ANNUAL REPORT
OF
PROGRAM ACTIVITIES

DIVISION OF RESEARCH GRANTS
DIVISION OF RESEARCH SERVICES

FISCAL YEAR 1972

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE   NATIONAL INSTITUTES OF HEALTH

DRG

DRS

ANNUAL REPORT

OF

PROGRAM ACTIVITIES

.S. National Institutes of Health. DIVISION OF RESEARCH SERVICES

Fiscal Year 1972

R
853
U56163
1972

DRG

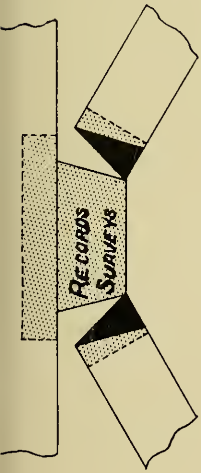
DRS

HOW TO USE THESE SEPARATORS

Use one page for each separation.

Select appropriate tab, add further identification if desired, and cover it with scotch tape.

Cut off and discard all tabs except the one covered by tape.



TABBED SEPARATOR SHEET
Form HEW-69
(3-56)

D
R
S

TABLE OF CONTENTS

Page No.

Summary 1

Office of the Director 3

  Grants Associates Program 5
  Information Section 7

Administrative Branch 9

Career Development Review Branch 11

Institutional Relations Branch 15

Research Analysis and Evaluation Branch 19

Research Grants Review Branch 23

Statistics and Analysis Branch 33

SUMMARY

The Director and Deputy Director continued their contact with the scientific community and grantee institutions by participating in a variety of scientific and national organization meetings held during the year.

The Research Grants Review Branch experienced an even heavier workload than ever before, processing 23,239 competing and non-competing applications with more than 85 percent of the applications receiving initial scientific review by the Branch.

A paper entitled, "Who reads your project-grant application to the National Institutes of Health," (Federation Proceedings, Vol. 51, No. 1, January-February 1972) prepared in the Branch formed the basis for a panel discussion at the spring meetings of the Federation of American Societies for Experimental Biology.

Several workshops and conferences were sponsored during the year by the study sections in a variety of fields to examine the state of the art.

Services from the IMPAC system were expanded by the Statistics and Analysis Branch in several areas including equipment accountability and the indirect cost management system.

A feasibility study to investigate the automation of RGRB's Investigator Record Card files by use of computer-generated microfilm files, initiated in the past fiscal year, was completed. The system will go into effect during FY 1973.

The CRISP system, implemented last year by the Research Documentation Section, was fully operative during the period under review with a 68 percent increase in requests for services.

The eleventh edition of the Research Grants Index was published in May.

An evaluation project was developed to measure the training impact of NIH research grant programs by using certain NIH Research Grant Manpower Survey findings.

There was a 1.2 percent decline over the previous year in fellowship applications received and processed by the Career Development Review Branch; 14 percent increase in competing training grant applications, and 4.3 percent increase in research career development award applications. Thirty-four percent of all applications were referred to the Health Services and Mental Health Administration.

The Division's employee training program, inspired by the NIH Affirmative Action Plan, was stepped up considerably in this, its third year. Requests for training were received from 267 employees. Twenty employees are attending the Upward Mobility College.

To meet the Civil Service Commision's request for annual reports on training programs, including total employees, man-hours expended, and total cost by grade, sex, and category of training, a computerized reporting system was developed.

Responsibility for gross screening of applicants was transferred from the Grants Associates Board to the Civil Service Examining Panel.

A completely new appropriation and allotment code structure for commitment reports was introduced into the IMPAC system at the start of the fiscal year.

OFFICE OF THE DIRECTOR

The Director presented papers at four scientific meetings during the year under review: The Association of Independent Research Institutes, Palo Alto, California, September 23-24, 1971; the Grants Associates Seminar held at the National Institutes of Health, February 28, 1972; California State University and Colleges, San Francisco, California, March 13-14, 1972, and the Business Officer Section-Northeast Regional Meeting, Association of American Medical Colleges, San Juan, Puerto Rico, May 3, 1972. The Director also attended the meetings of the National Council of University Research Administrators, Washington, D.C., November 14-16, 1971; the Council of Graduate Schools, Washington, D.C., November 2-4, 1971; and the Western Association for Graduate Schools, Tempe, Arizona, March 5-7, 1972.

The Deputy Director substituted for Dr. Lamont-Havers at the 13th Annual Meeting of the National Council of University Research Administrators, Washington, D.C., November 14-16, 1971, speaking on recent developments at NIH. On February 10, 1972, he spoke at the Annual Meeting of the Chemical Society of Washington, D.C. on how to apply for research grants, and why research grant proposals are turned down. The Deputy Director also attended the 82nd Association of American Medical Colleges meeting, Washington, D.C., October 28-November 2, 1971, and the Annual Meeting of the Federation of American Societies for Experimental Biology in Atlantic City, New Jersey, April 10-13, 1972.

The organizational changes approved on March 8, 1972, were put into effect with the establishment of the Office of Associate Director for Scientific Review, the elevation of the Institutional Relations Section to branch status, and the establishment of the Administrative Branch.

Twelve new administrative forms were produced and four existing forms were revised by OD staff members for internal use.

Application forms for the research career program Type 1 and Type 5 awards were revised, together with accompanying instructions; and a combined application form was developed for Type 5 (continuation) research grant (2490) and training grant (2499-2) applications. Revision of the Type 1 research grant (398) application form has begun, and at a later date the fellowship application form will also be revised.

The Division has been finding it increasingly difficult to recruit lower grade personnel. A recurring reason is the location of the Westwood Building and the lack of easily accessible public transportation.

To complete the 3-year term of the first DRG-EEO Counselor, who is on leave of absence to attend the University of Maryland, another staff member was appointed in October 1971 for a 1-year term. In preparation for the duties, the incumbent attended a course in equal opportunity counseling at the U.S. Civil Service Commission. Additional training was provided by the NIH-EEO Office in a workshop on the role of the EEO counselor.

Approximately 50 employees were counseled during the period October 1971 through May 1972. Not all of the problems were within the five basic responsibilities of EEO, but were of sufficient importance to the employee to require counseling.

Through the DRG orientation program, new employees and others interested attended a session where the structure and functions of the EEO program at NIH were explained, and the role of the EEO Counselor was discussed. Plans are being made to disseminate this information to all DRG employees.

The revised Affirmative Action Program was reviewed with the DRG branch chiefs, and meetings were held with them to review their responsibilities in implementing the Program.

The Counselor attended the EEO Council meetings. She has also attended the meetings of the DRG-EEO advisory group, the Training Opportunities Program Committee, as a non-voting member acting as liaison between the Council and the TOP Committee.

The former DRG-EEO Counselor and the former Chairman of the TOP Committee each received awards presented by the Division for outstanding work in EEO.

A training officer with responsibility for all employee training within the Division was appointed by the Director.

The Division's employee training program, inspired by the NIH Affirmative Action Plan, was stepped up considerably in this, its third year. The program covers both short-term needs that are directly and immediately applicable to the employee's work, and long-range career plans.

A computerized reporting system was developed to enable the Division's Personnel Office to submit annual reports to the Civil Service Commission on the DRG training programs. Information submitted includes total employees, total man-hours expended on the programs, and total cost by grade, sex, and category of training.

At the present time, 20 employees are attending the Upward Mobility College. Requests for training were received from 267 employees. Of the 791 courses requested during the year under review, 398 were completed, 48 are in progress and 27 approved courses are pending. Many of these courses are computer-related. Training has been provided by the National Institutes of Health, interagency, and non-Government organizations.

An employee handbook, "DRG is People," was produced to help DRG employees become aware of how their duties relate to DRG's overall mission, and for use in conjunction with orientation programs for new employees.

"Project Dialogue" continued to be supported by interested staff members. Lunchtime workshops have been held for bridge, knitting, needlecrafts, decoupage, and creative candlemaking.

GRANTS ASSOCIATES PROGRAM

The Grants Associates Program graduated nine associates in Fiscal Year 1972 all of whom remained in the Public Health Service. Six new associates were appointed, bringing the total number of associates assigned to the program during the past year to 15. The peak number (9) of associates on board occurred in September. It is estimated that the authorized level of 10 associates will be in training during Fiscal Year 1973. The level of interest in the program continues to be high, stimulated, no doubt, by the present economic situation which has resulted in a decrease of opportunities for scientists in academic and industrial institutions.

During the past fiscal year 150 applications were received; 49 candidates were interviewed and 8 were invited into the program.

The Grants Associates Office continues to play a role in the placement of applicants in direct hire positions. As in the past, emphasis has been placed on the referral of minorities and women.

The procedure for selection of associates was modified this year. The responsibility for gross screening of applications was transferred from the Grants Associates Board to the Civil Service Examining Panel. This facilitates coordination between the Civil Service Panel and the Grants Associates Board.

D
R
S

INFORMATION SECTION

An increase in the number of special searches for NIH categorical support was noteworthy during the year. Such inquiries emanated from the Congress, special interest groups, and other Federal agencies. The backlog of such inquiries was so extensive in March that a search for the Department of Commerce on NIH dollar support of telecommunication for the past 10 years had to be performed manually by information staff to meet the due date for the report.

Inquiries most frequently made concern international fellowships, policy on the transfer of projects and equipment, the need for financial assistance at the predoctoral level, summer training programs, how to get grant support, and policy on patents and inventions. There has been a marked increase in the number of requests for investigator reports ranging from grants awarded in 1947 to the present time. Inquirers are referred to the investigators as NIH does not receive sufficient copies of reports for public dissemination.

Reprints of a paper by Dr. George N. Eaves, "Who reads your project-grant application to the National Institutes of Health?" published in Federation Proceedings, has been beneficial to the Information Section through eliminating the need for numerous lengthy letters in response to inquiries on application procedures and the review process. Approximately 4,000 copies of Dr. Eaves' paper were mailed by information clerical staff in March and April.

In addition to the monthly and annual publications for which the Information Section has responsibility, an organization and functional folder was produced to depict the reorganization of the Division. The proceedings of two meetings, "Bioengineering Approaches to Problems of the Spine," and "Problems of Assessment and Alleviation of Malnutrition in the United States," were edited and prepared for offset reproduction.

The Division's exhibit came out of moth balls for the first time since 1968 to be presented at the 56th Annual Meeting of the Federation of American Societies for Experimental Biology in Atlantic City, New Jersey, April 10-14, 1972. Refurbished to represent all NIH (excluding BHME) and staffed by professional personnel from most of the awarding institutes and divisions, the exhibit attracted more than 2,000 grantees and prospective applicants for consultation during the 5-day meeting. Approximately 500 requests for literature on support programs and the review process were channeled to the Information Office through exhibit personnel.

ADMINISTRATIVE BRANCH

Under the reorganization plan for the Division that was put into effect during the spring of 1972, the Office Services Section, Travel Section, Special Services Section, DRG Reference Room, Central Mail Room, Budget Office, and the office administering the scientific evaluation grants were amalgamated under a new administrative branch.

The Office Services Section mailed an average of 8,000 grant and award application folders and 9,500 miscellaneous packages each month during the period under review. The Section also continued to provide planning and assistance in accomplishing several major moves within the Division, and to maintain responsibility for the acquisition and maintenance of equipment, furniture and supplies, and printing services for Division personnel.

Over 5,000 travel vouchers were received and processed by the Travel Section for DRG personnel and consultants serving on the review committees. The Section also offered assistance to Division travelers in plotting itineraries, preparing vouchers, and obtaining tickets and travel advances.

The Special Services Section continued to provide typing and repetitive typing assistance to DRG, NIH institutes and divisions. Repetitive typing assistance (Flexowriter and Dura) increased slightly to approximately 4,500 jobs. Typing jobs included over 250 Summary Statements and about 100 statistical tables as well as several booklets and papers for publication. Section personnel have assisted in the Upward Mobility Program by teaching typing.

Scientific evaluation grants valued at over $1,300,000 were processed and audited during fiscal year 1972.

CAREER DEVELOPMENT REVIEW BRANCH

During the past year, the Branch has undergone a series of reorganizations as a result of which the staff has been reduced from 47 to 30 employees.

Receipt and processing of all types of applications during the 12-month period, April 1971 through March 1972, declined from 12,517 to 10,993, a decrease of 12.2 percent. The demise of the predoctoral research fellowship program accounted for most of this decline. Receipt of competing training grant applications showed an increase of 14 percent and receipt of competing research career program applications increased 4.3 percent. Of the total applications received in CDRB, 34 percent (3705) were directed to the Health Services and Mental Health Administration.

Research Career Program

During the first 9 months of this fiscal year the research career program experienced a net increase of 10 awardees, to 1114. A total of 164 awardees (K-3, K-4, and K-6) left the program (37 of these were early terminations). In this same period, 174 new awards were made: K-4: 163; K-7: 10; K-8: 1. The first K-8 awardee (Clinical Investigator) entered on duty in February.

The total number of NIH awardees on duty as of 3/31/72 was 1114, divided between programs as indicated below:

Research Career Award (K-6)	136
Research Career Development Award (K-3)	409
Modified Research Career Development Award (K-4)	558
Academic Career Development Award (K-7)	10
Clinical Investigator Award (K-8)	1

Procedures for the processing and administrative review of the new National Institute of Arthritis and Metabolic Diseases academic and clinical investigator awards (K-7 and K-8) in gastrointestinal diseases and nutrition were developed in cooperation with the extramural staff of the National Institute of Arthritis and Metabolic Diseases.

By the end of the first quarter of this fiscal year all of the institutes of the National Institutes of Health were using the DRG study sections for the scientific merit review of their applications. CDRB professional staff conducted orientation sessions for the study section executive secretaries and visited the DRG meetings in September and again in January to answer questions regarding the program and to furnish information on policy.

A revision of the policy brochure for the modified research career development award (K-4) was initiated. The first revision of the RCP application and its instructions was completed and is now ready for presentation to the NIH Forms Committee. The RCP staff, with the help of representatives from several of the institutes, is now revising the RCP continuation (Type 5) application and its instructions.

During the year, the Branch has been streamlining its processing and data capture procedures. Greater reliance is being placed upon S&AB print outs. Mailing procedures for continuation applications were partially computerized in April 1972. The labels and letters for the application kits are prepared by S&AB, and forwarded to the RCP Coordination Section for the completion of the mailing procedures. Currently, a study is underway with regard to eliminating, through the use of S&AB supplied information, the RCDA files. The results of this study should be available in the very near future.

Because for every 10 application kits requested, only 1 application is received by the NIH, an information flyer on the research career development award was developed. This two-page flyer was distributed nationally in September 1971. Institutional officials can remove the coupon at the bottom of the second page and send it to the CDRB for an application kit.

Training Grants

Two significant new forms used in the training grant program were developed during the year. Both of these forms are in a sense revisions of existing forms, but their use will be expanded into new areas. CDRB played a major role in the development of each with the Assistant Chief, Training Grants, chairing one drafting committee and the Acting Chief, CDRB, the other.

The first of these two forms was the application for non-competing (Type 5) training grants. The new form developed is to be used for research grant applications as well as training grants. This fact made necessary the closest cooperation between CDRB and RGRB. It was also necessary to involve program officers from the awarding units who deal with both programs. The new form has cleared NIH and has been forwarded to OMB for approval.

The NIH has decided to revise the Training Grants Policy Statement in the near future. The present document is approximately 5 years old and several of the policies contained therein are now outdated and others are being changed. An initial rough draft was prepared by CDRB. As soon as the Research Grants Policy Statement revision is finalized, a formal draft of the Training Grant Policy Statement will be prepared.

During the year the Branch carefully studied the processing activities relating to the training grants program. These studies were undertaken as a direct result of recommendations made by an NIH Task Force which looked at all processing within the DRG. As a result, several changes have been made and others are planned for the future, e.g., many of the CDRB training grant files have been retired and the possibility exists that most, if not all, of the files remaining may be discarded in favor of routine computer print outs to be supplied by the Statistics and Analysis Branch. Also, computer assistance in the actual processing of Type 5 training grant applications should be under way early next fiscal year.

The Coordination Section has continued to acquire fiscal data from Training Grant Award Statements. This data relating to the categories of costs appearing on the award is not captured by S&AB; therefore, CDRB is the only source for NIH-wide data. The section now has comparable data from 4 fiscal years available for inquiry and analysis.

Fellowships

The Fellowships Coordination Section audited approximately 1000 Predoctoral Report of Expenditure forms for NIH and NIMH with an additional savings of $17,167 that otherwise would not have been returned to DHEW.

The "Reference Data Book on NIH Research Fellowships FY 1971" was revised for this fiscal year's operations. This book contains 36 various statistical reports comprising 55 pages. The booklet, "Research Fellowship Awards for Study Abroad" was compiled and issued as of September 30, 1971. This booklet is distributed to U.S. Embassies abroad, the State Department, and other Government agencies.

Program and review process changes have necessitated a revision of the fellowship application materials. In the near future a revised draft will be circulated for comment. Then a subcommittee will be established to review comments and to prepare the final draft for submission to the NIH Forms Committee.

A stipend survey (postdoctoral and special) is being conducted among the various Government agencies and the leading private foundations. It appears that several agencies have increased their postdoctoral and special stipends considerably. In any event, current information will be available soon.

Problems Encountered

One serious problem was duplication of applications. Duplicating ran approximately a month late over the last deadline. This meant that CDRB had to xerox two copies for the awarding units to mail to their consultants. This problem was incurred also by Research Grants Review Branch and resulted in several meetings sponsored by ADERT and appropriate awarding units and DRG personnel. Actions taken at that time should obviate a recurrence of this problem.

APPLICATIONS RECEIVED IN CDRB
TRAINING GRANTS, RCPs, and FELLOWSHIPS
April 1971 through March 1972

COMPETING - Types 1, 2, 3

	TG	RCP	FE	TOTAL
NIH	974	617	2174	3765
HSMHA [1]	836	84	666	1586
OTHER [2]	42	0	1	43
TOTAL	1852	701	2841	5394

NONCOMPETING - Types 4, 5

	TG	RCP	FE	TOTAL
NIH	1642	899	898	3439
HSMHA [1]	1691	152	276	2119
OTHER [2]	41	0	0	41
TOTAL	3374	1051	1174	5599

TOTALS

(All Components)

Competing	5394
Noncompeting	5599
GRAND TOTAL: April 1971 through March 1972	10993

---

[1] HSMHA: HS-MH-EM-OH-RL
[2] OTHER: EC-EP-AP-ES-FD

INSTITUTIONAL RELATIONS BRANCH

This Branch is principally concerned with certain nonfiscal obligations of grantee institutions. At the moment these obligations relate to compliance with the DHEW policy on protection of human subjects, the National Institutes of Health policy on animal welfare, and the provisions of Title VI of the Civil Rights Act. The Branch has responsibility for the content of two publications, the NIH/DRG Newsletter and the Notice of NIH Conferences. In addition, the Branch administers pilot studies in institutional prior approval, institutional distribution of renewal and continuation applications, and is developing procedures necessary in the implementation of PL 85-934 (authority for expenditure of funds through grants for support of scientific research).

Protection of human subjects at risk

At the beginning of FY 1972, the Branch had completed public review of the "Institutional Guide to DHEW Policy on Human Subjects" and began issuance of copies to grantee organizations. Over 21,000 copies have been distributed.

The Branch is renegotiating all active Public Health Service general institutional assurances of compliance covering 759 grantee institutions to bring them into compliance with DHEW policy. This procedure should be completed by July 1, 1972. Branch staff have also cooperated with the Food and Drug Administration, Health Services and Mental Health Administration, National Institutes of Health, Office of Education, and Social and Rehabilitation Service staff to develop procedures to implement Manual Chapter 1-40 in their respective agencies and to identify programs to which the policy is applicable. A classification system has been developed for projects identified by review groups as involving ethical problems or potentially hazardous procedures. Of 549 such projects identified through the beginning of FY 1972, approximately 50 percent were concentrated in three areas: drugs and biologicals, biopsy, and catheterization. The Branch continues to follow up on council action to insure that council criticism of institutionally approved projects involving human subjects is conveyed to institutional review groups.

Care and Treatment of Laboratory Animals

The NIH policy on this subject was issued June 14, 1971, with an effective date of December 31, 1971. All institutions on record as having NIH grant, contract, or award support have been contacted about conformance with the policy; this represents a total of 2,955 institutions. Assurances of compliance with the policy have been received from 449 institutions, while 1,062 have indicated that currently they do not use the covered species in NIH-supported programs. Some 1,324 institutions remain to be heard from, including a number which are known to use animals in NIH-supported activities. The NIH policy stipulates that projects involving the use of warm blooded animals will be supported only at those institutions which have filed the necessary assurance statement with NIH. The coverage of the policy is restricted to the six species (dogs, cats, monkeys, guinea pigs, hamsters, and rabbits) identified as "warm blooded animals" by the Animal Welfare Act. As of February 23, 1972, Under Secretary Veneman approved the development of a DHEW policy to be based on the NIH policy. The Branch will provide staff support for the Office of Grant Administration Policy in this development.

Biohazards

In March 1971, the Branch began filing initial review group summary sheets identifying biohazards described in applications. Following review of this data on March 10, 1972, the Associate Director, Extramural Research and Training, instructed the Branch to develop implementation of an ECEA report calling for a more positive NIH attitude toward safety problems evident in research grant proposals.

Equipment Accountability

Since full implementation of PL 85-934 has been delayed until July 1, 1972, the Branch has moved slowly in putting together the materials necessary to identify grantees that are either institutions of higher education or scientific organizations whose primary purpose is the conduct of research. Arrangements have been made with the Office of Education and the Internal Revenue Service to obtain tentative listings of institutions falling into these two categories.

Pilot study to improve the speed of handling of renewal and continuation applications

To examine the feasibility of routing application kits through one control point, three institutions agreed to act as reception and distribution points for renewal and continuation application kits normally sent directly to principal investigators. In early FY 1972, invitations were sent to an additional 14 institutions. Eleven accepted. After 4 months' experience, invitations were sent to 12 more institutions. Two have accepted, four have declined, six have not been heard from. Those declining the invitation, including both State and private institutions, have cited cost considerations as the principal factor. None of the participants have described any serious administrative or operational problems in connection with the study. All of the participants seem satisfied that the procedure has distinct benefits as contrasted with direct mailing.

NIH/DRG Newsletter

During the year, envelope mailing of the Newsletter was abandoned, and printing of mailing indicia directly on copies was begun. In mid FY 1972, the original mailing list, based on an old OFM institutional listing and including over 3,000 addresses, was discarded and mailings were placed on a demand basis. Copies are sent to institutional officials only. Circulation has decreased from over 8,000 copies to approximately 1,300 but is slowly building up again.

Notice of NIH Conferences

The Branch continues to publish the quarterly "Notice of NIH Conferences" for internal distribution. The publication assures that all NIH components are made aware of NIH-supported conferences and of their results.

Institutional Prior Approval Program

This program, now limited to 128 institutions, will become inoperative on June 30, 1972, when the proposed revised NIH policy statement will become available and will incorporate most of the program's provisions.

D
R
S

RESEARCH ANALYSIS AND EVALUATION BRANCH

The Research Analysis and Evaluation Branch produced several reports analyzing trends in NIH extramural programs and continued to examine in depth a variety of biomedical disciplines and scientific areas in relation to the overall support provided by NIH. As a service to the research institutes and divisions, the Branch now codes all research contracts according to the Central Scientific Classification System.

Among the reports dealing with trends in extramural research grant and training grant programs were the following:

Funding Patterns for Competing R01's under $20,001 in Direct Costs

Funding Patterns for Competing R01's under $35,001 in Direct Costs and under $35,001 in Total Amounts Awarded

Short-Term Trainees Supported by NIH Training Grants and General Research Support (DRR)

Analysis of Recent Trends in Extramural Research Programs and Recent Budgets

Equipment Expenditures on Extramural Research Grants

NIH Commitments to Research Grants in Relation to Program, Dollar Size and Age of Grants

New Principal Investigators on Traditional NIH Research Project Grants

The topics covered in the reports above were used in briefings of OADERT by the Deputy Director of DRG and Chief of RAEB. Analysis of NIH regular research program budgets for similar kinds of briefings was a new task assigned to the Branch this year.

Reports analyzing the NIH support of various biomedical disciplines included the following:

Report for the National Academy of Sciences' Future Directions in Chemistry Committee

Data on 43 Subcategories of Chemistry for the Office of Science and Technology

Estimate of NIH Support of Extramural Research in Immunology

NIH Grants and Awards to Schools of Pharmacy, FY 1971

Analysis of Grants on Transplantation, FY 1971

D
R
S

Orthopedic Research and Prosthetic Materials Research, FY 1971

Ethical, Legal or Moral Implications of Biological or Medical Research

In the latter three reports RAEB served as intermediary for defining the request, but the data were produced essentially by the Research Documentation Section from the CRISP system. For the purpose of analyzing various biomedical research disciplines, the Central Scientific Classification System has proved to be a useful tool although not the final word on the subject. The Branch has a continuing responsibility for reporting data on chemistry to the National Academy of Sciences and to the Federal Interagency Chemistry Representatives. The Chief of RAEB represented NIH at two meetings of chairmen of chemistry departments at the American Chemical Society convention in Boston.

Reports of a more substantive nature included the following:

NIH Extramural Grant Support of Research on Diseases and Abnormalities Occurring in the First Five Years of Life

Response to Ralph Nader Request for Data on the Ten Leading Causes of Death among the Adult Population in the United States, and an Estimate of the Amount of NIH Research Relevant to these Diseases

The report on childhood diseases was completed and forwarded through channels to DHEW. This study showed that over a recent 5-year span (FY 1966-1970) approximately $300 million was expended on projects considered to be explicitly concerned with health problems affecting children under 5 years of age. The level of support in FY 1970 was over $70 million funded through more than 1,000 grants in the NIH extramural programs. The kinds of research involved ranged from projects dealing with the basic biochemical defects in genetic diseases to clinical studies of diseases in infants and young children. In addition to the main section of the report showing the amounts of support in various explicit child disease problems, a second section consisted of four in-depth studies of problems (selected renal diseases, cystic fibrosis, injury and trauma, and lead poisoning) in early childhood to illustrate the magnitude and relevance of basic biomedical research supported by NIH. The whole report is being fragmented into smaller sections for dissemination to the NIH community.

The response to the Ralph Nader request for information on the ten most important causes of death dealt with some of the inherent complexities and the overlapping nature of NIH research programs. Data provided by the institutes were coordinated by RAEB and interpreted in the text accompanying the data. The importance of research efforts to lessen morbidity resulting from important categories of diseases affecting the population was also stressed.

Backgrounders for the Secretary in connection with his visits to the Albert Einstein College of Medicine, Yeshiva University and to Presbyterian-

University of Pennsylvania Medical Center were prepared by RAEB. In narratives for speeches, the salient features of NIH support to those institutions were highlighted.

In nearly all of the reports mentioned above, the Branch relied heavily upon data from the CRISP and IMPAC systems of the Statistics and Analysis Branch. In a number of instances information was gathered from program analysis officials of the institutes and from other components of DHEW.

RAEB, in cooperation with S&AB, assisted OADERT and NIH women executive secretaries get their study of "possible sex bias in the review of research grant applications" started by determining the sex of approximately 27,000 applicants for traditional research project grants in the FY 1967-1971 period. The methodology employed in this project will probably be useful in assigning sex on training and fellowship applications.

RESEARCH GRANTS REVIEW BRANCH

The Research Grants Review Branch referred and reviewed an even larger number of research grant applications than in fiscal year 1971.

The Branch processed 23,239 competing and non-competing applications during the year under review, not only for the National Institutes of Health but also for the Health Services and Mental Health Administration. Of these applications, more than 14,000 were assigned for technical merit review. Approximately 76 percent of the competing applications received were assigned to the National Institutes of Health. In spite of the special programs and increased reviews by institute committees, more than 85 percent of the applications have been provided initial scientific review by the Branch.

The distribution of applications processed this year is shown in the table on page 34.

Added responsibilities have come to the Branch during the past year, which have increased workloads and deadline pressures in the Referral Office of the Branch as well as in the study sections. Many specialized programs have been continued and initiated; for example, the SCOR program of the National Heart and Lung Institute and the clinical allergy centers program of the National Institute of Allergy and Infectious Diseases have been continued; the sickle cell anemia program of the National Heart and Lung Institute, the genetic center program of the National Institute of General Medical Sciences, and the target organs program of the National Cancer Institute, etc., have been initiated. Other programs have been expanded, for example, the alcohol and drug abuse program of the National Institute of Mental Health, and the periodontal disease program of the National Institute of Dental Research. Applications for each of these programs require either special handling and/or the creation of new procedures. The Branch continues to review applications for the Veterans Administration and has initiated review of fellowship applications for the National Institute of Environmental Health Sciences. The Branch continues to provide special services for specific programs, for example, the special dental research awards program of the National Institute of Dental Research, the resource related research projects program of the Division of Research Resources, the resources improvement grant and resources project grant programs of the National Library of Medicine, the small grants program of the National Institute of Mental Health, and some aspects of the research career development awards program. To accommodate these responsibilities with concurrent reductions in staff, changes in procedures have been made and more changes are being considered. Feasibility studies are underway for utilization of a microfilm data file. From these studies, new procedures will undoubtedly be developed. A review of the guidelines for institute/bureau/division and study section assignment has been initiated.

The Chief of the Branch continues to have many NIH-wide assignments related to extramural programs. He continues as one of the two Division of Research Grants representatives on the Executive Committee for Extramural Affairs (ECEA). He served again on committees concerned with the development of the NIH Manual issuances. In one such assignment, he was chairman of a committee on biohazards which developed an NIH Manual issuance to be released shortly. He still serves as the National Institutes of Health representative to the Division of Chemistry and Chemical Technology of the National Research Council. This year Dr. Schiaffino and Dr. James supplied information relating to NIH's role in the support of chemistry to the chemistry section of the National Academy of Sciences.

In the spring of 1972, recommendations of the Human Embryology and Development Study Section concerning the use of the human fetus in research were adopted in modified form by the National Institutes of Health.

Following developmental work done in this Branch during fiscal year 1971, a uniform normalization procedure for priority scores of applications reviewed by initial review groups was adopted by NIH and put into operation during this fiscal year. Normalized priority scores as well as the untreated priority scores are provided on computer-printed reports to institutes and divisions.

A comprehensive new Handbook for Grants Assistants was issued in September 1971. Although designed for use by grants assistants in the Research Grants Review Branch, it has been requested by many other initial review groups in the Public Health Service.

An article written by Dr. George N. Eaves, Research Grants Review Branch, formed the basis for a program on the project grant application presented on April 10, 1972, at the annual meeting of the Federation of American Societies for Experimental Biology. The session was chaired by Dr. Ronald Lamont-Havers and included among the speakers Dr. Eaves and Dr. Helen Hofer Gee of this Branch.

Entitled "Who reads your project grant application to the National Institutes of Health?" the article appeared in Federation Proceedings 31:2-9 /1972/. It was written to help scientists prepare better grant applications. The basis for the article is the assumption that authors of project grant applications could prepare more effective applications if they knew for whom they were writing. The article provides a brief outline of the structure of the NIH and presents a detailed account of the peer review process. Topics include a description of the process of assignment of applications to appropriate study sections for scientific review and to institutes and other awarding units for possible funding, an account of the actual review by study sections and national advisory councils, and a depiction of how a study section meeting is conducted. Two sections of the article that should be particularly helpful deal with the preparation of an application and with the common reasons for disapproval of applications.

A report resulting from one of last year's conferences was published in the fall of 1971: "Conference on Mechanical Surface and Gas Layer Effects on Moving Blood," Proceedings of the Federation of American Societies for Experimental Biology, September-October 1971. This conference, included in last year's Annual Report, was sponsored by the Surgery A and B Study Sections and the National Heart and Lung Institute.

Another report resulting from a fiscal year 1971 conference sponsored by these same study sections became available during the year under review. The publication, entitled, Proceedings of Workshop on Bioengineering Approaches to Problems of the Spine, was published by the Division of Research Grants.

A publication not mentioned in last year's annual report resulted from a 1970 conference sponsored by the Dental Study Section and the National Institute of Dental Research: "Supplement: Conference on Specific Questions Related to Periodontal Diseases," Journal of Dental Research, March-April 1970, Volume 49, Number 2, Part 1.

Proceedings of a workshop-conference held in September 1970 were published in book form in 1971: Cellular Mechanisms for Calcium Transfer and Homeostasis, edited by George Nichols, Jr., and R. H. Wasserman, Academic Press, New York and London, 1971. The conference, sponsored by the General Medicine B and Dental Study Sections, the Atomic Energy Commission and the Easter Seal Foundation, was described in last year's annual report.

Study sections sponsored and organized a number of workshops and conferences to survey the status of research in their areas, enhance the review competence of their reviewers, and stimulate research in neglected areas.

Two conferences planned during fiscal year 1971 were held in conjunction with the August and September study section meetings. A large workshop on "Interaction of Steroid Hormones with Target Tissues" was convened August 27-28, 1971, in New York City by the Endocrinology Study Section. The workshop brought together 130 scientists to discuss and evaluate the present state of knowledge of tissue uptake, localization, and cellular effects; metabolism and binding receptors, and early effects on cell processes. Thirteen 30-minute talks were presented in four workshop sessions by leading experts in the field of steroid hormone action. Each talk was followed by a 15-minute question and answer period and each session ended with a 45-minute open discussion during which members of the audience were invited to present data. Presentations covered recent work on tissue uptake, localization and binding to receptors, and early biochemical effects of estrogens, androgens, progesterone, aldosterone, and cortisol. Although minor discrepancies arose, a general two-step mechanism appears to operate in the target cells for each of these steroids, whereby the hormone first interacts with a cytoplasmic protein and the resulting complex then enters the cell nucleus. The relationship of binding of steroid hormones to nuclear receptors and the very early increases in the rates of synthesis of specific proteins and RNA's to nuclear binding and generally increased biosynthetic activity received considerable attention.

On September 15, 1971, at the NIAID Rocky Mountain Laboratory, Hamilton, Montana, the second fall conference was held. Sponsored by the Tropical Medicine and Parasitology Study Section and the Rocky Mountain Laboratory, NIAID, the conference was on "Dynamics of the Interactions of Arthropod Vectors with their Hosts and with Infectious Agents."

The 41 participants met to review and appraise the present status of research on host-vector-parasite interactions and on determinants of field transmission of important disease agents and their spread in vector and host tissues. These problems require further investigation for information critical to the development of more effective disease treatment, control, and/or prevention measures.

Attention was concentrated on two problem areas in disease agent transmission through variations in arthropod-host-parasite systems of arboviruses, filariae, hemorrhagic fevers, malaria(s), plague, schistosomes, spotted fever(s), tick fever(s), tick paralysis, tularemia, and other infections. These two topic research areas were: (a) the types of host response to arthropod bites or to parasite invasion and the effects of the kind of host responses on the success of transmission of disease agents present in the vectors, and (b) the effects of intra- and interspecific variations in arthropods themselves on their vector capability for transmitting disease agents.

After the extensive considerations of the conference, it was concluded that much more needs to be known about the host response to arthropod bites and their immunological significance. Many of these responses are already known to vary according to the duration of contact between the arthropod and host, the antigens and host species involved. Characterization of these reactions, the substances responsible for them, and the subsequent general and local reactions of the host remain to be defined over a period of time in a critical manner.

The following aspects were identified as high priority areas of research with public health implications: delineation of the immunoglobulin response, the antibodies of the immediate and delayed hypersensitivity type reactions, and the requirements for desensitization of individuals; closer study of sequential cell types and tissue reactions both in skin site of bite and adjacent lymph tissues with tracing of the arthropod antigens inoculated into host tissues through use of the most sensitive methods available; the isolation and characterization of arthropod oral secretions and possible contaminative microorganisms contained therein, and observations of genetic variability in the host and vector susceptibility and reaction to parasite invasion and its significance in the success of disease agent transmission.

In general it was recognized by the conferees that much more in depth study of the critical determinants in the infectious process in arthropod vector-parasite-host systems is needed. Such research holds potential for development of novel approaches to desensitization of individuals allergic to insect bites and for disease agent control through protection of man and animal against biting vectors and for effective control of vectors through genetic manipulations. The many unknowns in continuing disease outbreaks, and changing patterns of infectious agent dissemination by arthropods, point to present lack of sufficient understanding of factors and mechanisms involved. It was recommended that these problems should be investigated by a multidisciplinary team approach for their early solution. Publication of a report of the meeting in a journal is planned.

Study sections sponsored five workshops in conjunction with the January 1972 study section meetings. The Reproductive Biology Study Section sponsored the earliest of these, "Biology of the Testis," held in Bethesda, January 8-9, with 14 participants and 20 observers attending. Chemistry of the male genital tract and the seemingly endless number of possibilities of producing physiologic (or immunologic) blocks to fertility are constant questions in research grant applications. In the male the testis is involved in every aspect of endocrine function, both normal and abnormal. More minutely are such important things as the epididymis, vas deferens, vasa efferentia, seminal vesicles, prostate, and other structures under control of testicular activity. Capicitation, a physiological state, is apparently under the dual control of the male and female genital tracts, and is necessary to fertilization. Spermiogenesis, a most intricate process of cell growth and maturation, is not fully understood. Sperm transport, both in the male and female tracts, continues to be an incompletely understood factor in reproduction and sterility.

The first subject presented covered type A spermatogonia, undifferentiated, and their propagation. These cells maintain a constant self-population, and they also serve to form, through Aal spermatogonia, the first generation of differentiating spermatogonia. This presentation was the source of extended group discussion.

Other subjects presented included the following: (1) the organization of seminiferous epithelium and boundary tissue of tubules with emphasis on the blood-testis barrier; (2) the function of Leydig cells in the production of androgens; (3) the metabolic basis for the steroid producing testicular function; (4) deleterious effects on spermatogenic function of elevated temperature, hormone imbalances, certain chemical agents, and some nutritional conditions; (5) RNA involvement in nuclear differentiation and the transition of basic proteins; (6) testicular macromolecules and their possible function as antigens upon injection into unlike species; (7) pituitary and gonadal hormonal control of spermatogenesis in studies using rats; (8) control of canine testicular steroidogenesis and consideration of the transport of steroids by spermatic venous blood or by the spermatic lymph system; (9) the biogenic pathways in the developing testis, including some evidence for a biological "clock" in the Leydig cells; and (10) human testicular function and morphophysiologic and genetic considerations. In a round table discussion the thesis was advanced that a male contraceptive which allowed normal development of normal sperm, but which inhibited sperm delivery would seem to be the most desirable.

On January 13, the Bacteriology and Mycology Study Section sponsored a workshop on "Current Bacteriology and Mycology Topics" which was held in Bethesda with 25 scientists participating. Four broad areas were discussed by the speakers and participants: (1) clinical infectious disease in the U.S. and the world; (2) recent progress of work in cellular immunity; (3) the relationship of ultrastructure of pathogenic organisms to disease; and (4) current problems in syphilis and gonorrhea. In the United States salmonellosis is not getting the attention it should. It is estimated that there are probably 2 million cases per year. Reporting of the disease is inadequate. Data are also lacking on the prognosis of persons with bacteriuria. There are perhaps 3 to 3½ million cases of urinary tract infections, and it is not known how many will proceed to serious renal disease. Worldwide, gastroenteritis caused by enteric pathogens remains one of the main causes of death.

In the field of cellular immunity much more has to be learned. Since humans are exposed to fungal pathogens throughout life and little clinical disease is seen, cellular mechanisms of resistance may perhaps be the prime line of defense. Another area of concern is the treatment of burn patients wherein there is a reduced immunological response. Further studies are necessary to enhance resistance of such patients when they are most susceptible to infections.

The mechanisms of host susceptibility and/or virulence of microbial agents might be partially explained on a molecular level by studying the changes in host metabolism caused by the presence of microbes. Similarly, differences in microbial metabolism within a host cell or tissue may lead to the factors responsible for virulence.

The incidence of both syphilis and gonorrhea is on the increase. It is estimated that there were 2 million cases of gonorrhea in 1970 in the U.S. and 2½ million cases in 1971. It is the second most communicable disease (the common cold is first). For both gonorrhea and syphilis, effective vaccines and reliable serological tests for diagnosis still need to be developed.

A Bethesda workshop on "Plasma Amino Acids" sponsored by the Nutrition Study Section was attended by 25 participants on January 19. The use of total parenteral feeding in clinical medicine and the addition of amino acids to foods to be ingested orally by man has stimulated interest in (1) the transport and utilization of amino acids; (2) the significance of the serum aminogram; (3) the potential for amino acid imbalance; (4) the effect of amino acids on polyribosomes of the brain and liver; and (5) the relationship of amino acids load to blood glucose concentration, growth hormone and insulin release and satiety. Topics presented and discussed were: (1) amino acid transport in kidney, intestine, and brain; (2) effects of the route of administration of amino acids or protein hydrolysates on serum amino acid levels in infants and adults; (3) the serum aminogram in starvation, diabetes, and exercise; (4) dietary disproportions of amino acids--their influence on satiety; (5) polyribosomes--their role in protein synthesis, and their responses in the liver following amino acid administration.

One of the conferences planned during fiscal year 1971 took place on January 19, 1972, in Bethesda. The workshop, sponsored by the Toxicology Study Section, was concerned with the "Introduction of Toxicology Information into Basic Textbooks." Thirty participants met to survey biology and basic science textbooks of elementary, high school, and college levels, for their content of toxicological information, with the purpose of increasing the amount of information now supplied.

The morning session consisted of the presentation and discussion of several technical aspects of toxicology with the object of familiarizing non-toxicologists with some of its major activities and its place in science. For example, a presentation was made concerning the place in nature of endogenous poisons, their protective value to certain creatures and the methods by which their enemies may overcome their inhibitory effects. Further development was made of how much interplay might affect the evolution of certain creatures. It was intended that this and the other presentations would lay the groundwork for discussion of the usefulness of the inclusion of several aspects of toxicology in texts of general biology.

In the afternoon session, authors of high school and college texts presented the types of materials now used and noted the difficulty of including details of all aspects of science. They did note the probable usefulness of a toxicology emphasis in relation to many problems of popular interest, such as pollution, drug misuse, widespread use and misuse of man-made poisons, such as pesticides, and the problems regarding preservation of a proper ecological balance.

It was conceded by all participants that increased development of toxicological topics in textbooks would be important, useful and interesting.

A more detailed summary of the day's work is planned for publication in journals of Education and Science.

The fifth January conference, sponsored by the Computer and Biomathematical Sciences Study Section, was a "Workshop on Artificial Intelligence Applications in Biomedical Computing." On January 26-27, in Bethesda, fifty participants, including several of the Nation's leading contributors to artificial intelligence research, participated in a series of seminars on some of the important biomedical research applications of the techniques of artificial intelligence. The use of heuristic programming in the study of human problem solving as exemplified in the work of Newell and Simon was presented, and the Dendral system at Stanford, which generates molecular structural hypotheses from mass spectral data, was described. Recent work on speech understanding was discussed, as were problems of meaning in natural language communication and computer understanding of meaning as exhibited in interactive interviewing programs.

Three conferences were associated with the April study section meetings. A conference on "Ultrasonics in Medicine" brought together 30 scientists who reviewed this subject on April 13-14. This conference, held in Bal Harbour, Florida, was sponsored by the Radiation Study Section, which has seen a quadrupling over the past 2 years of the number of grant applications in this rapidly advancing field. The use of ultrasonic waves in medicine has increased tremendously over the past few years and it has proved of value in both the diagnosis and treatment of disease. Amongst the latter may be listed its use as a source of focussed, deep-seated heat in physical therapy, a method of producing small deep-seated brain lesions for the cure of certain neurological diseases and lastly, as a method for attaching detached retinas. Regarding the diagnostic applications, ultrasonics can be used not only to specify distances to various interfaces such as the midline of the brain or to surfaces of various internal organs and tissue inhomogenieties, but the reflections from such interfaces and/or inhomogenieties can be used to create images similar to radiographs. Transmission ultrasonic holographs are also possible and may be the future imaging technique of choice. All these images, however, are caused by tissue properties much different from those used in creating radiographs, and, hence, represent a new diagnostic modality. Further, sequential images can be made not only of moving objects, but changes in reflected sound frequency with object motion (Doppler Effect) allow an even more unique diagnostic tool, particularly in cardiology.

At the moment, research interests lie with (1) instrument development in adapting many of the more sophisticated radar techniques to ultrasonic imaging; (2) improving diagnostic accuracy and potential of various ultrasonic images and image manipulations; (3) utilization of the absorption coefficient of various tissues as an even more powerful visualization parameter; (4) investigating the apparent synergism between sound, heat, and ionizing radiations in neoplastic tissue; (5) examining the biologic effects of low intensity ultrasound (diagnostic levels) including suspected chromosonal aberrations; and (6) creating images with Doppler shifted sound.

At the conference, the following topics were presented and discussed: (1) recent advances involving physical aspects of ultrasound; (2) mensuration and imaging; (3) medical applications; and (4) the future of ultrasound research. Areas for further research were delineated. Results of the conference will be published.

The Pathology B Study Section assembled a large conference in Bethesda, April 18 and 19, on "Neoplasia and Cell Differentiation." About 100 participants met to discuss the current research on carcinogenesis and differentiation based on the most recent studies of the molecular mechanisms involved in both processes and their mutual relationship. Among the participants were some of the members of the Cell Biology, Molecular Biology, Pathology A, and Pharmacology B Study Sections.

Speakers presented the following topics: (1) studies on chromatin structure; (2) the non-histone proteins in chromatin structure and function; (3) cell cultures--models for tumor promotion; (4) quantitative studies on chemical carcinogenesis in vitro; (5) study on fetal and adult isozymes in liver systems; (6) alterations in melanin systems in human melanoma; (7) suppression of malignancy and a differentiated function in melanoma cells by a 5-bromodeoxyuridine; (8) biochemical mechanisms involved in morphogenesis and functional differentiation of mammalian reproductive organs; (9) oncogenic viruses in embryogenesis; and (10) neoplasia and differentiation as translational functions.

The third April conference was entitled "Workshop on Magnetic Resonance," sponsored by the Biophysics and Biophysical Chemistry A and B Study Sections. Nearly 60 scientists participated in this workshop held on April 19-20 in Pasadena, California. Among the subjects covered in lectures and round table discussions were these: (1) chemical shifts, coupling constants, and techniques; (2) application of magnetic resonance to nucleic acids; (3) the mapping of active sites of enzymes, enzyme kinetics, etc.; (4) applications of nuclear magnetic resonance to the structure of proteins; (5) NMR study of condensed systems--membranes--cell water; (6) electron paramagnetic resonance; (7) the electron spin resonance of transition metals; and (8) future instrumentation.

Plans have been made for two conferences in conjunction with the September 1972 study section meetings. The Tropical Medicine and Parasitology Study Section will have a workshop in New Orleans, Louisiana, on September 13 entitled "Human and Zoonotic Filariasis: Current Concepts and Directions of Future Studies." The presentations and discussions will have bearing on further definition of this group of prevalent diseases, and possible suggestions of new and improved methods for their diagnosis, treatment, and control. Although worldwide, several hundred million persons are infected with filarial parasite(s), there remains a dearth of knowledge about human infections with these parasites.

Latest advances in mammalian cell-culture techniques as applicable to investigations in molecular biology is the subject of a small workshop--seminar to be sponsored by the Molecular Biology Study Section in the latter part of September 1972.

APPLICATIONS PROCESSED BY REFERRAL OFFICE, RGRB
Fiscal Year 1971: March 16, 1971 - March 15, 1972

COUNCIL		NOV.71	MAR.72	JUNE 72
		COMPETING		
Types 1, 2, 3	NIH -	3,479	3,389	3,995
	HSMHA -	752	775	1,388
	EPA -	207	-	-
	FDA -	38	48	36
TOTAL		4,476	4,212	5,419
Construction		10	24	24
PL 480		10	14	8
Career Development included in NIH Count				
Subtotal		4,496	4,250	5,451
		NON-COMPETING		
		(All 3 PHS components)		
Type 5		3,516	2,161	2,346
Interim-Regular & Cross Fiscal		311	387	321
Subtotal		3,827	2,548	2,667
		TOTALS		
		(All 3 PHS components)		
Competing		4,496	4,250	5,451
Non-Competing		3,827	2,548	2,667
TOTAL		8,323	6,798	8,118
Grand Total for FY 72 (Competing and Non-Competing)				23,239

STATISTICS AND ANALYSIS BRANCH

The Statistics and Analysis Branch continued to expand and improve its services to IMPAC users during the past fiscal year although forced to work within restrictive budgetary and personnel controls. It points with pride to its record in extending reporting services, in meeting user deadlines, and in accomplishing system expansion by increased data capture, and by initiation of technical improvements to the CRISP and IMPAC systems.

The Branch continued its support of the NIH Affirmative Action Plan for Equal Employment Opportunity through an active employee training and development plan. Employees were encouraged to participate in training courses and seminars, and, as appropriate, in the Upward Mobility College Training program.

The individual training efforts, major accomplishments, and significant activities of the Branch are discussed below under the responsible section.

Data Processing Section. Services from the IMPAC system were expanded in several areas: equipment accountability, indirect cost management system, and mailing of continuation applications for training, research career, and fellowship programs.

Relating to the first area, equipment accountability, DPS will prepare quarterly institution listings of all grants whose project periods are scheduled to terminate in that quarter, and will prepare mailing labels for transmittal. These listings, along with a supply of NIH Form 1754, "Equipment Acquired with NIH Grant Funds," will be mailed to the responsible grantee institutions. Completed forms will be returned to DRG and distributed to the awarding unit for appropriate action.

In the second area mentioned above relating to the OFM Indirect Cost Management System, the link between the DRG IMPAC System and the OFM Grant Payment System was modified to include the transfer of indirect costs generated by the OFM Indirect Cost Management System. Via this link, all new calculations and adjustments of indirect costs for NIH research grants are transferred bi-weekly to DRG and stored on a grant-by-grant basis in IMPAC system records.

Additionally, as a result of a special joint CDRB and SAB study, computer services were extended to the Career Development Review Branch to assist in the mailing of continuation applications for the research career, training, and fellowship programs. These services include the monthly identification of applicants to receive continuation and renewal applications and the preparation of mailing labels, instruction sheets, and institute/division notification listings. Services are expected to provide considerable man-hour benefits over the former manual methods for processing and mailing renewal applications for these programs.

The feasibility study to investigate the automation of the Research Grants Review Branch's Investigator Record Card files by use of computer-generated microfilm files initiated in the past fiscal year was completed in June. Under the proposed microfilm system, DPS will furnish RGRB, for referral purposes, a completely updated microfilm file every 2 weeks containing all active research and research career grants, grants which terminated within the past year, and pending applications. Upon receipt of a new or competing application the staff in the Project Control Unit of RGRB will search the microfilm file and make a copy of appropriate background data, which will be forwarded with the application to the referral officer. The provision of a computer generated microfilm file eliminates the need for manual updating of the investigator record cards and provides a means for RGRB to continue processing an increased number of applications within the limited time provided in spite of serious personnel shortages. It is expected that this system will be adopted in fiscal year 1973.

Use of optical scanning for creating new and competing application records in the IMPAC system has proven highly successful. It was possible under this system to process and fully verify approximately 11,000 research, training, fellowship, and special BHME and Mental Health program applications for the June cycle. This could not have been accomplished with the on-board personnel within the required time frame even with an unlimited use of overtime. The optical character processing has been expanded to incorporate the data input into several other areas, the updating of records to the Master File of the IMPAC System, and the creation and modification of records for the Project Address File, a file of about 37,000 records. Based on demonstrated success with optical processing as a data-input system, further expansion is being investigated.

The Programming Unit of DPS has developed a method of accessing its on-line IMPAC files to retrieve and format master records. Any authorized user can now initiate an inquiry by a remote IBM 2741 terminal and receive the requested information on the terminal, or, if desired, this information may be directed to either a remote printer or to the high-speed printers at the DCRT Computer Center.

In line with the Branch's training policy, 32 people from the Data Processing Section attended training courses both within NIH at the DCRT Computer Center and in other areas, and outside NIH at the Institute for Advanced Technology, CDC, the Civil Service Commission, the IBM Training Center, and American University. In addition, five people from the Data Capture Unit of DPS are participating in the Upward Mobility College Training Program.

Research Documentation Section. CRISP System. The CRISP System (Computer Retrieval of Information on Scientific Projects), implemented last year, was fully operative this fiscal year, with a 68 percent increase in requests for services. This independent retrieval system, on disk storage, contains data about the scientific aspects of research grants and contracts programs of the various health component agencies of DHEW. It has the query capability of providing information ranging from a straightforward listing of grants pertaining to a single scientific subject term to a compendium of projects relating to any number of subject terms using combinations of "and," "or," "not" search logic. Queries are answered in a variety of formats, incorporating whatever fiscal, grant identification, or subject matter items the user requests. Several modifications were made to the query program during the year among which is the capability of retrieval on program of institute code.

The scientific data used as input to the CRISP System are the indexing items which are selected to prepare the annual editions of the *Research Grants Index*. A WYLBUR terminal has been installed recently so that the Section can explore the possibility of entering new grants input data by WYLBUR instead of the optical character recognition method used heretofore. The Section plans to use this as a temporary retrieval medium for new grants, thus cutting down the lead time for computer access to this type of information by several months.

Research Grants Index. The eleventh edition of the *Research Grants Index* (NIH Publication no. 72-200, 2 vols.) was published in May 1972. This year the *Index* was prepared from a magnetic tape extracted from the CRISP System and composed by the Government Printing Office's Linotron equipment.

The *Index* describes over 17,000 currently active biomedical research grants and contracts. In Volume I of the RGI, project titles are listed under some 6,500 keyword subject headings which are arranged alphabetically. Volume II has three sections. The first section contains the grants and contracts in project-number order; the second section is a separate listing of research contracts; and the last section is an alphabetical list of principal investigators.

Copies of the *Index* are distributed annually to information personnel, scientists and scientist-administrators within the Government, and to grantee institutions. The *Index* is also on sale by the Superintendent of Documents, U. S. Government Printing Office.

Automation of Mailing List for the Research Grants Index. Personnel of the Section recoded and reformatted about 2,000 mailing addresses to prepare for automation of the RGI mailing list by the Optical Addresser equipment in the NIH Print Shop. A premailing and updating of the distribution list was made by this system. In addition, the Section applied primary and secondary supplemental codes to the individual addressee cards to enable the RDS to make a variety of statistical studies of the recipients of the *Research Grants Index*. Considerable savings in personnel time will be realized in future mailings of the Section's publications.

Medical and Health Related Sciences Thesaurus. *Revised Edition*. A revised edition of the *Medical and Health Related Sciences Thesaurus* was published this year, and about 300 copies were distributed on a request basis. (The MHRST is used as the indexing authority list for the *Research Grants Index*. It is also one of the four component files of the Section's retrieval system, CRISP--Computer Retrieval of Information on Scientific Projects.)

Vocabulary Compatibility Studies.--Initiated this year were comparability studies of the Medical and Health Related Sciences Thesaurus with the vocabularies of the National Library of Medicine and the NIH Central Scientific Classification Codes. The purposes of these studies are (1) to construct compatible hierarchical codes for inclusion in the MHRST to improve retrieval and indexing capabilities; and (2) to analyze the extent of compatibility or convertibility among similar coding systems. So far, 12 disease categories have been completed, such as infectious diseases, musculoskeletal diseases, hemic and lymphatic diseases, diseases of nutrition and metabolism. These studies will continue next year covering other areas of the MHRST vocabulary.

Other activities of the Section this year included the compilation of statistics on multiple grants (MO and PO) projects, showing total number of subprojects, and various other statistics. The Section is working on more detailed analyses of these projects to include bound compilations of the vocabularies used for indexing multiple grants, an alphabetical index of individual investigators and their individual bibliographies, in conjunction with the titles of the subproject research as included in the Research Grants Index.

Training and Presentations. Personnel of the Section participated actively in the various training courses offered this year at NIH. Over 14 courses were attended by members of RDS staff, including one person who attended the Upward Mobility College for two semesters.

The Chief of the Section gave several orientation lectures during the year to staff of DRG and other NIH groups.

Statistical Analysis and Surveys Section. The primary function of the Statistical Analysis and Surveys Section is the collection, storage, computer retrieval, presentation, and analysis of data on the extramural programs of the NIH and PHS for use in policy consideration, program planning, program analysis, and program management. In addition, the Section is responsible for the coordination of responses to inquiries about the extramural programs received from the Executive and Legislative Branches of the Government and non-Government sources. The major activities and outputs of the Section during FY 1972 are described in the following sections.

Manpower Analysis. A report containing selected findings of the NIH Research Grant Manpower Survey was provided the Office of Management and Budget. Outlines were developed and work proceeded on four detailed reports based upon the survey findings: "Paid Employment and Personnel Expenditures on NIH Research Grants," "Characteristics of Students and Postdoctorals Paid for Working on NIH Research Grants," "Principal and Key Investigators on NIH Research Grants," and "Students and Postdoctorals Working Without Pay on NIH Research Grants."

As part of the FY 1972 NIH Health Evaluation Program, an evaluation project was developed--and approved--to measure the training impact of NIH research grant programs by using certain NIH Research Grant Manpower Survey findings. A contractor was selected, a project outline developed, appropriate statistical models selected, and a preliminary report prepared.

Publications. One volume of Statistical Items was published this year: Number 12.1, Indirect Trainees Supported by NIH Research Training Programs, FY 1965 - 1969 Funds.

The following volumes of the annual multi-volume series of PHS Grants and Awards were issued:

(1) A preliminary volume of NIH research grants, FY 1971

(2) PHS Grants and Awards: NIH Training, Construction, Medical Libraries, and Summary Tables, Part II, FY 1970

(3) PHS Grants and Awards: HSMHA, FDA, and EHS, Part III, FY 1970

(4) PHS Grants and Awards: NIH Research Grants and Research Contracts, Part I, FY 1971

Data for the pocket reference book, Basic Data Relating to the NIH -- 1972, were compiled in cooperation with the NIH Office of Program Planning. This publication presents information on the programs and resources of the NIH.

Other publications by the Section included: The Research Career Program Annual Report for FY 1971, the Monthly News Release of NIH Grants and Awards, the Fellowship Annual Report for FY 1971, and the Extramural Research Trends and Highlights Report for FYs 1967-1971.

Reporting Activities. There are several major reporting activities which are recurring or cyclical and consume a large portion of the man-hours available in this Section. The annual survey conducted by the National Science Foundation entitled Federal Funds for Research, Development and Other Scientific Activities is coordinated and prepared by this Section for the entire NIH. In general, the survey covers all the NIH intramural and extramural research activities for the past fiscal year, with estimated obligations for the next 2 future years by performer, field of science, geographic area, basic and applied research and development, and combinations of the above. A segment of the report is also devoted to Scientific and Technical Information Activities.

The CASE Report is an annual survey on support to institutions of higher education and other nonprofit organizations. The NIH response to this survey is coordinated and prepared by this Section. It requires an institution-by-institution report of all NIH extramural support by program for most nonprofit organizations with an individual report for each health professional school. In addition, data by field of science grouping are also requested for institutions of higher education, by program.

The HSMHA portion of this survey was also prepared by this Section for those programs which are regularly processed by DRG.

Obligations for Medical and Health-Related Research and Training Activities is an annual survey of all Government-sponsored medical research and training. The NIH response to this survey is also coordinated and prepared by this Section and requires data on intramural and extramural research and development by field of science, performer, program, and state. Additional NIH data required include manpower statistics related to graduate training grants, fellowships, and research career program awards by degree sought, by institution, by field of science and by institutional vs. individual support.

At the beginning of each review for research and training grant applications, statistical reports are prepared which present data on the number and dollar value of applications received for review. The presentation is by institute, fiscal year of support, and type of application. Copies are distributed to each institute/division. In addition, statistical tables showing summaries of initial review group actions on research and training grant applications are prepared twice during each review cycle for use by the Office of Financial Management, the institutes/divisions, and the Career Development Review Branch, DRG.

Commitment Reports. A completely new appropriation and allotment code structure was introduced into the IMPAC system at the start of the fiscal year. To effect this change, all prior coding for these data items was eliminated from the system. New codes, effective at the start of FY 1972, were entered retroactively for all FY 1971 awards in file. This new code structure voided existing IRS routines formerly used to prepare Annual Commitment Reports for the OFM and institutes/divisions.

At the request of OFM, a new query routine was developed to produce a simplified Commitment Report for FY 1972 research. Refinements to these procedures are anticipated for the FY 1973 report.

Inquiries. The Section responds to hundreds of requests for information each year from Federal agencies and nongovernmental organizations. These requests are for statistical and analytical information concerning the NIH grant and award programs as well as for data on the characteristics of PHS grantee institutions.

The inquiries range in complexity, as measured by man-hours, from several hundred to less than one per project. Many of these requests are satisfied by data contained in existing but unpublished reports. However, the IMPAC system remains the primary data source and the Inquiry and Reporting System (a computer software facility) the primary method for data extraction, manipulation, and hard-copy presentation of the information requested. About 7,000 queries were processed through the Inquiry and Report Systems for this purpose during FY 1972.

Institutional Research. The Section has the responsibility for establishing and maintaining the Institution Profile File (IPF). The IPF is the central registry of names, locations, geographic and other selected data for organizations participating in the Public Health Service extramural programs. This file is the single source for organizational information established to assure uniform reporting and to eliminate the necessity for storing similar information in individual grant and award files. In FY 1972 over 1,500 new institutions were added to the IPF. The IPF now contains about 16,000 records on institutions participating in NIH programs as well as in those of the Food and Drug Administration and the Health Services and Mental Health Administration.

Retrieval Methodology. Three IMPAC Inquiry and Reporting System (IRS) courses were offered by the Section. Twenty-five persons attended the first, or basic, course. Of these, 11 were from DRG. The second course was attended by 17 persons from BHME. The third course covered more advanced applications. IRS is the primary instrument for extracting and reporting IMPAC data.

About 15 consultations are handled each day for DRG and institute/division personnel needing assistance in debugging queries, developing more advanced queries, and applying new techniques.

Retrieval Applications and Procedures ("RAP") has been developed as an informal, technical handbook to provide users with accurate information and instructions on how to apply new or more efficient retrieval procedures, and to correct recurring IRS problems. About 50 copies have been distributed, primarily in DRG.

Training. During the past fiscal year 24 of the Section's personnel attended training courses and seminars offered within NIH with several attending outside courses at the Institute for Advanced Technology, the USDA Graduate School, the Civil Service Commission, the University of Virginia, American University, and the Government Printing Office. One employee is attending the Upward Mobility College Training Program.

Graphic Arts. Approximately 880 pieces of graphic art work were completed in FY 1972. This work included: cover designs, charts, certificates, slides, signs, visuals, special exhibits, and illustrations for flyers and handbooks.

ANNUAL REPORT

OF

PROGRAM ACTIVITIES

DIVISION OF RESEARCH GRANTS

Fiscal Year 1972

D

R

S

D

R

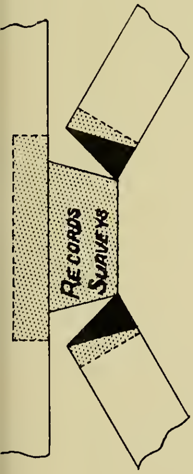
S

HOW TO USE
THESE SEPARATORS

Use one page for each separation.

Select appropriate tab, add further identification if desired, and cover it with scotch tape.

Cut off and discard all tabs except the one covered by tape.



TABBED SEPARATOR SHEET
Form HEW-69
(3-56)

DIVISION OF RESEARCH SERVICES

Report of Program Activities
July 1, 1971, through June 30, 1972

CONTENTS

Page

Division of Research Services 1

Biomedical Engineering and Instrumentation Branch 9

Individual Project Reports
1. Pharmacokinetics 23
2. Development of Metal Complex Compounds for Control of Tumors. 26
3. Biomaterials 28
4. Tumor Growth on Semipermeable Membranes. 30
5. Fluorometric Monitoring of Cortical Surface Metabolism 32
6. Nuclear Magnetic Resonance Techniques for Biochemical Analysis 33
7. Psychophysiological Conditioning via Aversive Stimulation. . . 35
8. Ultrasonic Measurement of Cardiac Dynamics 37
9. Viable Cell and Neuron Activity Monitoring in Tissue Culture . 39
10. Atraumatic Electrical Sensing in Brain Cortex. 41
11. Biomechanical Concomitants of Head Injury. 42
12. Autologous Blood Reinfusion. 44
13. Automated Precision Fluorometry. 46

Environmental Services Branch 49

Library Branch. 65

Medical Arts and Photography Branch 73

Veterinary Resources Branch 79

Individual Project Reports
1. Chronic Respiratory Disease of the Laboratory Rat. 95
2. Tyzzer's Disease 97
3. Pasteurella In Gnotobiotic Rats. 99
4. Fluorescent Antibody Technique as a Serologic Means of Detecting *Babesia Canis* 101
5. Genetic Analyses and Development of New Strains for Biomedical Research. 103
6. Development of Diets for Laboratory Animals. 105
7. A Comparison of Physical and Hematologic Characteristics of Puppies Fed Diets Containing 9%, 8%, and 6% Fat 107

NATIONAL INSTITUTES OF HEALTH

DIVISION OF RESEARCH SERVICES

Report of Program Activities
July 1, 1971, through June 30, 1972

A. Objectives

The Division of Research Services provides scientific, technical, and engineering services to support and further the research programs of the National Institutes of Health. All services are geared to the needs of Institute programs. Therefore the Division makes a continuous effort to keep informed of Institute plans. The DRS organization, staffing, and functions are adjusted accordingly to maintain an effective program of centralized services.

B. Current Programs

A broad range of central research support services and products are provided by the Division and its five branches: Biomedical Engineering and Instrumentation, Environmental Services, Veterinary Resources, Library, and Medical Arts and Photography. The current programs of the Division include the following:

1. Biomedical engineering of methods, systems, instruments, and materials
2. Instrument fabrication and maintenance
3. Development of an environment conducive to quality research and compatible to patients, staff, and community
4. Production of bacteriologic and tissue culture media
5. Preparation of sterile glassware
6. Production of genetically defined rodents and rabbits
7. Quarantine and conditioning of dogs, cats, and primates
8. Dog blood donor colony
9. Maintenance of farm animals
10. Animal surgery and recovery
11. Animal health services
12. Library and computerized bibliographic services
13. Foreign language translation
14. Still and motion picture photography
15. Graphic arts services and exhibits design
16. Medical illustration and model making

C. Program Progress and Accomplishments

1. Appointment of a New Director

Dr. Roger Estep, former Executive Assistant to the President, Howard University, was appointed Director of DRS effective December 1, 1971.

Dr. Estep replaced Dr. William B. DeWitt, who died suddenly on August 8, 1971. Dr. Joe R. Held, Chief, Veterinary Resources Branch, served as Acting Director during the interim.

2. Management Analysis Projects

With the assistance of the Administrative, Budget, and Personnel Offices, the Management Analysis Office developed a system which projects the month-by-month employment effect of anticipated personnel actions. This system, the Projected Average Grade and Employment System (PAGES), provided management with accurate forecasts which were essential in the administration of recruitment and promotion actions throughout the Division. It also assisted the Division in the identification of errors in Agency and Departmental systems.

Several Branches and the OD expanded their use of the Data Reporting System (D*R*S) during the second year of its operation. The Director made frequent reference to individual B/I/D service graphs as one factor in the formulation of Division budget plans. The Photography Section used both service graphs and expense graphs to carefully analyze its first year of fee-for-service operation, and to plan for service continuity during their upcoming laboratory renovation. The Budget Office and several of the Branches used the system to keep track of full-time permanent employment trends. The Rodent and Rabbit Production Section continued to monitor animal issues, and also found that the graphs provided an early warning of problems with data collection months before they might have been indicated by OFM financial systems.

The Management Analysis Office added several new features to the D*R*S. Data from the Photography Section was brought into the system through an automated interface with the Office of Financial Management. A Secondary Item sub-system was installed to facilitate the preparation of summary graphs from any number of closely related primary items. Modifications to the Trend Report sub-system improved the visual quality and sequencing of the reports, and greatly reduced the required distribution effort. Finally, the Composite Item sub-system was revised so that most DRS Sections could obtain an overall graph of average manhours required by each Institute.

During the year, the Management Analysis Office provided the Branches with technical assistance and problem solving services through several other projects. The largest of these was a detailed survey of the BEIB job costing and inventory control system, which led to the formulation of new design specifications and to the development of several useful new management reports. Other projects included the annual financial review of all DRS Service and Supply Fund activities, the first comprehensive survey of all DRS data processing applications, and the second year of staff assistance in the preparation of the Annual Report via WYLBUR.

At the beginning of the year, Howard B. Kelly was named Management Analysis Officer for the Division. In March, he was also named ADP Unit Coordinator with administrative review responsibility for all data processing applications in the Division.

3. Equal Employment Opportunity

DRS held its Third Annual EEO Seminar in October. The main theme of the seminar was human relations in management. This was indicative of the need within DRS to re-examine supervisory employee/relationships.

The DRS goal was to develop mechanisms to produce a management attitude which would incorporate EEO as an integral part of every supervisor's job and not as a separate program. One significant outgrowth of the seminar was a method of supervisory performance feedback from employees.

In the first several weeks of his appointment, Dr. Estep held a series of conferences with all DRS employees. As one way of following up these conferences, the Division plans to organize a series of educational seminars for supervisors. These seminars constitute an on-going program. The target of these seminars is to help supervisors become more responsive to employee needs. These seminars will cover such topics as: leave regulations, Merit Promotion Plan, training and promotions, employee services, as well as numerous other personnel policy procedures and facts. This series has been planned with the basic idea that much administrative and personnel information can be communicated to employees.

In the area of employee training and development, the Director has appointed a Training Committee. The mission of the committee is to advise the Director on matters relating to employee training, with special emphasis on minorities and women, distribution of resources, methods of advertising training opportunities, and appropriate provisions for "fair-share" participation.

In addition to the above Affirmative Action projects, there will be a series of conferences with supervisors to define DRS's policies regarding the Plan, as well as point-by-point implementation procedures.

4. Employee Development

During FY 1972, DRS employees participated in over 29,000 man-hours of training, indicating an increase of about 50 percent over FY 1971. Of this total, approximately 18,000 man-hours were in courses offered by colleges, universities, manufacturing firms, and other non-Government educational activities; 4,800 in interagency courses conducted by CSC, GSA, or other Government agencies; and 7,000 in in-service courses offered by DRS, NIH, or other DHEW activities.

DRS employess continued to participate in the NIH Adult Education Program with several successfully completing their particular program. Five completed the Adult Basic Education Program and advanced to the High School Equivalency Program while eight received high school equivalency certificates. Currently, 19 employees are enrolled in the Adult Basic Education Program and 22 in the High School Equivalency Program.

The initiation of the Upward Mobility College at NIH this fiscal year has resulted in 32 DRS employees attending courses on campus during this period for a total of approximately 4,900 man-hours of class time.

DRS participation in the New Careers Program included the following training positions: Machinist Trainee, WG-5; Glassblower Trainee, WG-5; Medical Equipment Repairer, WG-6; and Library Technician, GS-6. In addition, a New Careers position (Library Technician, GS-2/3) was utilized by four Library Branch employees to receive three months training each in various library functions. Also during this period, two DRS employees were selected for the NIH Clerk-Typist Trainee Program and one for the DCRT Computer Operator Trainee Program.

During FY 1972, one DRS civilian employee has been enrolled at the University of California at Los Angeles in the year-long CSC Education for Public Management Program and one DRS PHS Commissioned Officer commenced a two-year program in comparative pathology at the University of California at Davis. Again this year numerous short courses were conducted by DRS Branches for selected employees of DRS and other B/I/Ds. The Environmental Services Branch conducted nine courses on such subjects as laboratory safety, hospital environmental control, sanitation techniques, insect and rodent control, waste water plant operation, and biohazards. The Veterinary Resources Branch conducted a comprehensive course on laboratory animal care for approximately 17 NIH employees, about one-third of whom were from VRB. Those who successfully complete the course and the subsequent examination will be certified as junior or senior animal technicians by the American Association for Laboratory Animal Science. The Biomedical Engineering and Instrumentation Branch conducted its annual course on the use of the ultracentrifuge for several B/I/D researchers.

5. Employee-Management Relations

The negotiated agreement between AFGE local 2419 representing non-supervisory employees in the MAPB remains in force. Certain minor ambiguities in the contract are being renegotiated at this time.

The AFGE, which also holds exclusive recognition in the NIH Library, is preparing proposals for contract negotiations in the near future.

6. Environmental Services

The Environmental Services Branch experienced an increased demand for environmental services during FY 1972. In industrial hygiene projects, major activities were oriented towards surveillance of air pollution sources, stack testing, and consultations in specific areas. Most of the consultations related to material toxicity, procedures and equipment needed for the safe handling, and proper disposal techniques to be employed.

A major portion of staff time was spent in consultation with NIH research personnel in assessing potential biological hazard problems and equipment use and procurement.

ESB expended major efforts in preparation of Environmental Impact Statements in conjunction with the Office of Engineering Services, ADA, for the Tri-Service Incinerator, NIH Master Plan, and the NIEHS North Carolina Research Facility. The Tri-Service Incinerator project was the most involved and time-consuming effort. This was the result of a court order suspending construction on the incinerator pending submission of an Environmental Impact Statement.

The program to eliminate mercury as an environmental pollutant at NIH continued. ESB established a monitoring program and in cooperation with OES developed traps for collection of mercury in the NIH sanitrary sewers.

During the year, ESB assumed total responsibility for the surveillance of the Clinical Center environment due to the phase-out of the Environmental Sanitation Control Department, CC.

The ad hoc Inter-Institute Technical Committee on Biohazards has completed its mission and submitted the final report to the Deputy Director for Science. The recommendations of the committee provide for the establishment of an NIH-wide biohazard program.

7. Biomedical Engineering and Instrumentation

The Branch professional staff was involved in a variety of research and developmental projects. These included surveys and modifications of surgical and patient care facilities to minimize electrical hazards; refinement of physiological monitoring and diagnostic procedures involving closed circuit video systems; extension of fundamental understanding of pharmacokinetic phenomena, especially as related to cancer chemotherapy and environmental contaminants; analytical and experimental investigation of the biomechanical concomitants of head injury; and development of improved techniques for monitoring CNS function.

Emphasis on economy has reduced the number of requests for fabrication of new research equipment and contributed to an increase in demands for maintenance and repair services.

The Scientific Equipment Rental Program has been improved and expanded and is now well accepted and often used by NIH investigators.

8. Animal Programs

The Laboratory Aids Branch has been redesignated as the Veterinary Resources Branch. This was done to better reflect its primary functions of providing NIH investigators with living models and life support systems for biomedical research and providing facilities and services related to the use of these models and systems.

At the request of I/D investigators, a number of new inbred strains were added to the genetic repository. This activity has continued to grow in importance in fulfilling NIH's needs, and as a resource of breeding nuclei and reference animals for the international scientific community.

The rodent and rabbit colonies represent the most diversified multi-species rodent collection maintained at any centralized facility. Diagnostic services for the rodent colonies were enhanced this year by the assignment of an experienced clinical veterinarian.

A rodent research facility is planned which will provide centralized professional care for animals under investigation and technical assistance to investigators.

A major change in the production of tissue culture media has contributed to a continued low rate of contamination.

The Animal Disease Investigation Service completed its first full year in operation, making a total of 128 calls to the various I/D's. Demand for this service continues to grow.

9. Library Services

Significant organizational changes have been beneficial to Library operations. Organizational locations of several units were shifted to improve effectiveness and coordination of related activities.

Bibliographic searching is now conducted through the National Library of Medicine's new MEDLINE computer system, as well as through its MEDLARS system which has been in use for some years.

As a result of feasibility studies of acquisition activities, DCRT's WYLBUR system continues in use for monograph order procedures, and the PHILSOM system was adapted for journal control procedure.

The Library Services Adviser program, initiated in 1971, provides expert guidance in obtaining resources and services available in the NIH and other libraries, which are pertinent to individual research needs. The program broadens and integrates the reference and bibliographic services of the Library. Increased attention will be given to expansion of this program.

The U. S. Court of Claims ruled against the Government in the Williams and Wilkins case relating to the photocopy service and the copyright law. The Department of Justice will prepare briefs to be presented to the full Court of Claims.

10. Medical Arts and Photography

Acquisition of additional photographic equipment and in-house modification of some processes has resulted in considerable savings in man-hours and faster services to the various I/D's. Increased availability of photomicroscopy is now possible as a result of two new photomicroscopes. A 70 mm copy camera system is now an integral part of the Branch photo production system. It has increased efficiency to a point where a projected savings of 480 man-hours per year is being realized. A faster and less expensive system for producing film positives for color slides and overhead projections has been established. In addition, the in-house modification of a microfilm process has resulted in a 380 man-hour savings per year.

The Branch has completed the NIDR work entitled "Studies of Oral and Pharyngeal Form and Function in Infants." This project spanned over four years, consuming a cumulative total of approximately 2,200 man-hours spent on medical illustrations and dissections. Also, a complete anatomy atlas of the male and female rhesus monkey was completed for a veterinary pathologist in the Department of Toxicology of NCI.

Design layout and architectural drawings were prepared and approved for the complete renovation of the Photo Lab area. Renovation construction will be completed in FY 1973.

DIVISION OF RESEARCH SERVICES

Summary of Branch Activities July 1, 1971, through June 30, 1972

BIOMEDICAL ENGINEERING AND INSTRUMENTATION BRANCH Dr. Lester Goodman, Chief

I. SUMMARY

Activities have been concentrated on functions that are important to the NIH mission but do not require large capital investments. These include, for example, surveys and modifications of surgical and patient care facilities to minimize electrical hazards, refinement of physiological monitoring and diagnostic procedures involving closed circuit video systems, extension of fundamental understanding of pharmacokinetic phenomena, especially as related to cancer chemotherapy and environmental contaminants, inquiry into the interactive mechanisms of implanted materials and living constituents, analytical and experimental investigation of the biomechanical concomitants of head injury, and development of improved techniques for monitoring CNS function.

A substantial amount of effort has been devoted to professional level consultation for all categorical NIH institutes and many other government agencies.

General emphasis on economy throughout the NIH has reduced the number of requests for fabrication of costly new research equipment and, simultaneously, contributed to a marked increase in demands for maintenance and repair services. The Scientific Equipment Rental Program has been improved and expanded; it is now well accepted and often used by NIH investigators.

Expansion of floor space in Building 13 and implementation of a new satellite in Building 35 have helped to overcome some deficiencies of long-standing.

Improved management practices, Equal Employment Opportunity, and implementation of the letter and spirit of the Affirmative Action Plan have become accepted matters of prime concern to all in BEIB. Machinist and glassblower trainee opportunities, with substantive growth potential, have been provided to disadvantaged individuals; a medical equipment repair technician completed a full-year course of specialized training and is now productively employed. Personal advancement through self-improvement has been emphasized via substantial enrollments in Basic Skills programs, Upward Mobility College, and local colleges and universities.

BEIB is well equipped to respond promptly and effectively to demands as they occur in the future.

II. BRANCH PROGRAMS

A. Objectives

To provide direct and consultative engineering support to clinical and biomedical research projects, including advice on systems analysis, experimental design, and synthesis of technical expedients.

To design, develop, fabricate, and evaluate special-purpose devices and systems not commercially available.

To maintain and repair scientific laboratory and clinical equipment.

To obtain and disseminate information on developments and improved production methods in the biomedical engineering and instrumentation fields.

B. Current Programs

The primary purpose of the Branch is to provide service and support to the intramural program of the NIH. BEIB activities, therefore, are identified with many of the individual programs that constitute the intramural research effort. The overall Branch program is best described as the coordinated effort of its operating units.

1. Instrument Fabrication

Production, modification, and minor design of medical equipment and instrumentation systems requiring special tools and skills in the electronic, electrical, glass, mechanical, optical, rubber, plastics, welding, and sheet metal categories.

2. Systems Maintenance

Maintenance and repair of biomedical equipment and instrumentation systems and instruction of technicians and scientists in the proper use and operation of especially complex instruments and devices.

3. Supply

Acquisition and disposition of materials, parts, and equipment required for Branch operations and maintenance of controlled inventory stocks and records.

4. Engineering and Applied Science -
Chemical, Electrical and Electronic, and Mechanical:

a. Direct and consultative professional services for fundamental and applied projects relevant to biomedical research and health care at the NIH.

b. Research, design, development, and evaluation related to new instrumentation and equipment.

c. Communication between NIH and the scientific community on engineering support to biomedical research and clinical practice.

5. Satellites

These technical support units, composed of selected engineers and technicians with appropriate shop facilities, are located in certain areas where it is beneficial to make typical BEIB support and service immediately available via a controlled degree of decentralization. They are responsive to demands of local programs and operate as integral parts of the resident team but are administratively responsible to the central Branch. Each is especially tailored to meet specific needs of the host institute or division. Satellite operation supplies the host with the advantages of a proprietary technical group and maintains the chief benefits of centralized resources.

C. Program Progress and Accomplishments

1. Technical Services

a. Instrument Fabrication Section

Workload during FY 1972 continued at a relatively stable level following a substantial decrease in the preceding year which resulted from restrictions and uncertainties in NIH intramural research funding. The section was able to meet demands, despite minor reductions in staff, by replacing a number of obsolete production machines with modern equipment. The Section completed approximately 4500 projects valued at $850,000 compared with 4300 projects valued at $890,000 in FY 1971.

b. Systems Maintenance

Emphasis on economy in the NIH intramural program resulted in a marked increase in demands for maintenance and repair of scientific equipment. SMS performed approximately 11,600 assignments at a cost of $960,000 compared with 9300 and $574,000 in the previous year.

New space made available for the Scientific Equipment Rental Program enabled improved organization and management of this rapidly growing activity. The number of instruments in the equipment pool is approaching 300; more than 100 items were rented to intramural investigators during FY 1972. Six thousand dollars' worth of new apparatus was added to inventories from operating "profits." Procedures for handling equipment and administrative transactions have been refined considerably with substantial use of ADP.

c. Supply Unit

Benefits of attention to improvement of operational and administrative procedures, in previous years, were manifested; the unit processed approximately 15,000 transactions compared with 13,000 in FY 1971; dollar value of material handled remained stable at $400,000 from FY 1971 to FY 1972.

2. Engineering and Applied Sciences

a. Chemical Engineering

Substantial progress in advancing knowledge related to chemical processes in the physiological context has been achieved via close collaboration with several intramural investigators. Research leading to a rational basis for predicting the pharmacokinetic behavior of the anti-cancer drug, methotrexate, was honored by the Ebert Prize of the Academy of Pharmaceutical Sciences of the American Pharmaceutical Association. This award honors the senior author of the best scientific report published during the preceding year in the Journal of Pharmaceutical Sciences.

Systematic mathematical analysis has produced a reliable method for estimating drug distribution patterns in large animals and man from small animal experimental data. A unique technique for growth of tumorous tissue *in vitro* enables detailed studies of growth behavior concomitants in living organisms. Metalo-organic complexes of the elements palladium and ruthenium, showing antineoplastic properties, have been successfully synthesized.

A significant contribution to analysis of metabolic reactions was achieved via completion of a new automated fluorometer capable of making differential measurements of enzymatically stimulated fluorescence of tissue sample solutions to within one part in 10^4 in the presence of background to signal "noise" level of 100 to one.

Work continued on investigation of properties of polymeric materials as they relate to biology and medicine, with emphasis on design, development, and evaluation of implant devices. Special attention was given to segmented polyurethane which is used with increasing regularity in physiological research; as a direct result of BEIB efforts, the material is now available on a commercial basis.

b. Electrical and Electronic Engineering

As implied elsewhere in the report, BEIB has completed a substantial number of new designs for electrical and electronic apparatus for the NIH research program. Significant progress was made in extending and improving previously developed techniques for utilizing fluoroscopic and X-ray data acquisition, processing, recording, and display in the context of cardiovascular research. New systems are being regularly used in the clinical arena, as well as the research laboratory, to obtain better understanding of cardiovascular dynamics and prosthetic heart valves in man during rest and exercise.

Collaboration with investigators from NIAMD and DCRT has improved methods for elucidating structural details of organic compounds containing carbon-13. Superconducting magnets to generate intense fields, coupled with on-line Fourier Transform analysis of pulse train responses and refined electronic circuitry, substantially improve the accuracy, precision, and sensitivity of NMR detection. The utility of ultrasonics, lasers, and cryogenics has been extended in several areas of biomedical research and clinical practice.

The Electrical Safety Program, conducted in collaboration with the Clinical Center Environmental Control Service group, expanded and improved its surveys of cardiac catheterization and intensive patient care facilities to assess electrical safety, detect potential hazards, and modify equipment and practices to maximize safety of patients and investigators alike. Excellent working relationships with the Clinical Center staff have been established. It is expected that the team will continue to work together, on a regular basis, to examine and improve the safety and effectiveness of all NIH patient areas.

c. Mechanical Engineering

Continued emphasis on close collaboration with research and service staff throughout the NIH resulted in several substantial developments of the year. Mechanization and automation of routine procedures received substantial emphasis. Efficiency and effectiveness of biological sample analysis were enhanced via several new automatic manipulator devices for aliquots and reagents. Distinct improvements have been achieved in methods for large-scale processing of laboratory glassware. These systems continue to reduce the cost and time of routine manual tasks and enable reallocation of manpower to more productive and challenging duties.

Considerable attention has been devoted to fundamental and applied research on the mechanisms of head injury. New testing apparatus has been designed to provide heretofore unobtainable information to enable improved analyses of relevant phenomena leading, eventually, to the rational design of improved protective devices. The state of the art in recording electrical signals from the brain, *in vivo*, has been markedly advanced with the development of new devices for precise atraumatic insertion of electrodes into cortical regions.

3. Technical Advances

BEIB has delivered a considerable number of special purpose devices and systems in support of research programs. Items of more than casual interest follow:

A GAS DISTRIBUTION SYSTEM uses sonic flow through adjustable restrictions to deliver prescribed mixtures of several gases to experimental animals over broad ranges of pressure and flow.

A SEGMENTED POLYURETHANE MEMBRANE aids in measuring episcleral venous pressure for detection of glaucoma.

A CONCENTRIC DEWAR OF UNIQUE DESIGN safely and conveniently contains cobalt-60 irradiated samples at liquid nitrogen temperatures.

HIGH RESOLUTION TEMPORAL AND SPATIAL ANGIOGRAPHY, with improved signal-to-noise ratios at low dose concentrations, is enabled by use of EKG synchronized scintillation detection and video mapping techniques.

A PHOTOELECTRIC SENSOR replaces a microscope eyepiece to improve studies of single cell motion patterns.

IMPROVED VIDEO FLUOROSCOPIC APPARATUS substantially enhances dynamic determinations of heart volume in vivo.

CARDIAC TISSUE SURFACE STRESS AND STRAIN measurements are produced with a position servo-controlled probe.

A PNEUMATICALLY-OPERATED BRAIN ELECTRODE INSERTER restrains lateral movement of a "thumbtack" type electrode to less than 0.001 inch during axial insertion, thus substantially reducing trauma.

A NOVEL AORTIC COUPLER, requiring no sutures, improves the speed, ease, and reliability of blood vessel anastomosis.

NEW NMR APPARATUS incorporates a superconducting magnet, controlled pulse excitation and Fourier Transform analysis to enable practical observation of ^{13}C nuclei in organic molecules.

A PHOTOMEASUREMENT SYSTEM provides rapid and accurate determination of transmission, absorption and fluorescence to facilitate studies of biochemical reaction kinetics with the Amino-Morrow stopped-flow technique.

A PORTABLE REMOTELY-CONTROLLED ULTRASONIC SENSING SYSTEM enables mapping of left ventricular phasic volume during exercise.

AN OPTICAL POSITION SENSOR of mass less than 0.4g and flat frequency response to 10 KHz is effective for accurate large stroke dynamic measurements on intact muscles.

A PSYCHOPHYSIOLOGICAL DATA ACQUISITION SYSTEM incorporates a variety of stimulus-response modes with automatic video display and tape recording of overt patient behavior and EEG to extend studies of epileptics.

A PIPETTE PROCESSING MACHINE automatically inserts or removes cotton plugs at the rate of 50 units/minute.

AN ALIQUOT TRANSFER APPARATUS transfers samples from microtitration plates to filter paper and automatically provides for saline washing, TCA lysing and ethanol rinsing; a 3-hour manual operation is reduced to 15 minutes.

ENDOCARDIALLY IMPLANTED PIEZOELECTRIC TRANSDUCERS enable *in vivo* ultrasonic tracking and measurement of left ventricular diameter in exercising experimental animals.

A HELMET-MOUNTED AVERSIVE STIMULATOR generates minor electrical shocks in response to excessive acceleration to curb self-destructive actions by autistic patients.

A CLINICAL FLUOROMETER monitors metabolic energy variations on cortical surfaces exposed during surgery.

A SEMIPERMEABLE POLYMERIC CAPILLARY TUBE BED serves as a matrix for *in vitro* growth and study of solid tumors.

4. Training

An effective professional and technical training program was essential in maintaining high quality support and service to the NIH program, especially during this year of reductions in staff levels. Forty-seven employees participated in 69 academic, administrative and technical courses. Twenty (250 man days) undertook formal education and training courses. Four (17 man-days) received specialized training on scientific equipment at manufacturers' facilities and at the NIH. Two members attended Basic Schools programs at the sub-high school level and five were enrolled in the Upward Mobility College.

The BEIB technician trainee program, in keeping with the principles of Affirmative Action, was expanded by addition of one machinist trainee and one trainee for the glassblower trade. These WG-5 employees are receiving academic instruction at Washington Technical Institute and Frederick Community College respectively, as well as intensive on-the-job training. One Medical Equipment Repairer trainee has returned from one year at the U.S. Army Medical Optical and Maintenance Agency, Denver, Colorado. He is now obtaining on-the-job experience to supplement and learn better to apply his newly acquired knowledge.

Under terms of Contract #NIH 72-C-175CC, BEIB/SMS and Beckman Instrument Company jointly conducted a course on the Model E Analytical Ultracentrifuge which covered basic operational techniques, relevant calculations, and interpretation of results. Dr. Marc Lewis, NEI, and Dr. Samuel Luborsky, NCI, were lecturers; Beckman Field Engineers provided instruction on practical operation. Seventeen scientists and technicians from NIH and other agencies attended.

A second course, under the same contract, was offered in Zonal Ultracentrifugation. Mr. Hunter Elrod, Duke University, was the instructor. Forty-eight attended lectures and demonstrations on Beckman Models L3-50 and L2-65B.

D. Program Plans

BEIB will continue to function in response to intramural requests for service and support. Since these consume very nearly all of its available time and resources, few changes in current patterns of operation can be contemplated. Several relatively minor innovative activities, already begun, should receive added emphasis during FY 1973. For the areas cited below, it is felt that meaningful work could be done without sizable increases in staff at this time. Obviously, given more resources, much more could be done. Each also represents areas of long-term commitment which could be readily enhanced if and when additional resources are forthcoming.

1. Implementation of a comprehensive biomaterials research, development, and evaluation program.

2. Activation of a university-BEIB cooperative program in biomedical engineering. Preliminary arrangements with the Howard University Chemical Engineering Department are under way.

3. Improvement and expansion of the Scientific Equipment Rental Program which is now well received and used by a rapidly growing number of intramural investigators.

4. Extension of the patient safety program now conducted primarily by BEIB electrical and electronic engineers, assisted by Systems Maintenance technicians with the cooperation of Clinical Center staff. Substantial progress has already been made; much more remains to be done.

5. Increased attention to collaborative intradivision research and development activities to improve the manner in which DRS, as a whole, serves and supports NIH. Closer interaction and collaboration among the five branches should be highly advantageous to all of NIH; particular projects should be defined and pursued.

6. Continuation and expansion of the technician training program under the auspices of the Affirmative Action Plan.

It is premature, at this time, to define particular new directions to be followed in FY 1974 and beyond. The implications of the plans cited above are long-term in nature and are certain to command considerable energies in the coming years.

E. Publications and Patents

1. Publications

Bennett, S.H., Hoye, R.C., and Riggle, G.C.: Intraoperative autotransfusion. The American Journal of Surgery, 123: 257-260, 1972.

Bischoff, K.B., Dedrick, R.L., Zaharko, D.S., and Longstreth, J.A.: Methotrexate pharmacokinetics. Journal of Pharmaceutical Sciences, 60: 1128-1133, 1971.

_____, Himmelstein, K.J., Dedrick, R.L., and Zaharko, D.S.: Pharmacokinetics and cell population growth models in cancer chemotherapy. Advances in Chemistry Series. (In press).

Boretos, J.W.: Communication to the editor - Tissue pathology and physical stability of a polyether elastomer on three-year implantation. Journal of Biomedical Materials Research. (In press).

_____: Long-term stability and compatibility of segmented polyurethane implants. In Proceedings of the 24th Annual Conference on Engineering in Medicine and Biology 1971, Las Vegas, Nevada, vol. 13. Washington, D. C., The Alliance for Engineering in Medicine and Biology, Dennis H. LeCroissette, Chairman, p. 212.

_____ and Wagner, F.R.: Communication to the editor: Particle fragmentation generated in pump sets. Journal of Biomedical Materials Research, 5: 411-412, 1971.

_____, Battig, C.G., and Goodman, L.: Decreased resistance to breathing through a polyurethane pediatric endotracheal tube. Anesthesia and Analgesia ... Current Researches, 51: 292-296, 1972.

_____, Detmer, D.E., and Braunwald, N.S.: Factors influencing longevity of low-profile prosthetic heart valves. Journal of Biomedical Materials Research. (In press).

_____, _____, and Donachy, J.H.: Segmented polyurethane: A polyether polymer, II. Two years experience. Journal of Biomedical Materials Research, 5: 373-387, 1971.

_____, Bourke, R.S., Nelson, K.M., Naumann, R.A., and Ommaya, A.K.: Technique for unilateral isolation of the subdural space in the intact primate. Journal of Neurosurgery, xxxv: 101-107, 1971.

Dedrick, R.L. and Zaharko, D.S.: Letter to the editor - Extrapolation of teratogenic effects. Chemical and Engineering News, 5-6, May 17, 1971.

_____, Forrester, D.D., and Ho, D.H.W.: In vitro - in vivo correlation of drug metabolism - Deamination of 1-β-D-Arabinofuranosylcytosine. Biochemical Pharmacology, 21: 1-16, 1972.

Detmer, D.E., McIntosh, C.L., Boretos, J.W., and Braunwald, N.S.: Polypropylene poppets for low-profile prosthetic heart valves. The Annals of Thoracic Surgery, 13: 122-127, 1972.

Dvorak, J.A. and Stotler, W.F.: A controlled-environment culture system for high resolution light microscopy. Experimental Cell Research, 68: 144-148, 1971.

_____, Clem, T.R., and Stotler, W.F.: The design and construction of a computer-compatible system to measure and record optical retardation with a polarizing or interference microscope. Journal of the Royal Microscopical Society. (In press).

Friauf, W.S.: A new electromechanical analogy. Instruments and Control Systems , 104-105, 1971.

_____: Letter to the editor. Medical Electronics & Data, 4-5, 1971.

Gabelnick, H. L. and Litt, M. (Eds.): Rheology of Biological Systems. Springfield, Ill., Charles C. Thomas. (In press).

Goldstein, S.R. and Harvey, A.C.: Gas flow control employing temperature and pressure compensation. Transactions of the ASME, Journal of Dynamic Systems, Measurement, and Control, 200-205, 1971.

Goodman, L.: Biomedical engineering--1971. Transactions of the ASME, Journal of Dynamic Systems, Measurement, and Control, 129-131, 1971.

Griffith, J.M., Schall, G.L., and Larson, S.M.: An improved detector for video systems used in radionuclide studies. Radiology, 100: 699-700, 1971.

Johnson, D.F., Lamontagne, N.S., Riggle, G.C., and Anderson, F.O.: Tape-controlled gradient elution chromatography system for steroid analysis. Analytical Chemistry, 43: 1712-1715, 1971.

Kelly, J.J., Bischoff, K.B., and Dedrick, R.L.: Diffussion models for the initial stages of thrombus formation on foreign surfaces. Irish Journal of Medical Science, 140: 368-378, 1971.

Ketcham, A.S., Hoye, R.C., and Riggle, G.C.: The laser in the surgical laboratory. Panminerva Medica, 13: 528-531, 1971.

LeRoy, A.F. and Morris, J.C.: The kinetics of hydrolysis of rutheniumnitrosyltrichloride. Journal of Inorganic and Nuclear Chemistry, 33: 3437-3453, 1971.

Marcus, M.L., Schuette, W.H., Whitehouse, W.D., Bailey, J.J., and Glancy, D.L.: An automated method for the measurement of ventricular volume. Circulation, XLV: 65-76, 1972.

Neel, H.B. III, Riggle, G.C., Myers, R.S., Ketcham, A.S., and Hammond, W.G.: Apparatus modifications for experimental cryogenic surgery of cancer. Cryobiology, 8: 501-505, 1971.

Perrine, T.D., Atwell, L., Tice, I.B., Jacobson, A.E., and May, E.L.: Analgesic activity as determined by the Nilsen Method. Journal of Pharmaceutical Sciences, 61: 86-88, 1972.

Peterson, J.I. and Young, D.S.: Preservation of urine with sulfamic acid in soluble packages. Clinical Chemistry, 17: 954-955, 1971.

_____, Friauf, W.S., and Leighton, S.B.: A high precision fluorometer for measuring enzymatic substrates in tissue. In Proceedings of the 24th Annual Conference on Engineering in Medicine and Biology 1971, Las Vegas, Nevada, vol. 13. Washington, D. C., The Alliance for Engineering in Medicine and Biology, Dennis H. LeCroissette, Chairman, p. 164.

Prusiner, S.B., Milner, L.S., Long, C.W., and Myers, M.L.: Vacuum manifold for rapid assay of enzymes using radioactive tracers and ion exchange chromatography. The Review of Scientific Instruments, 42: 493-494, 1971.

Riggle, G.C., Hoye, R.C., and Bennett, S.H.; An autologous blood reinfusion device - preliminary report. In Proceedings of the 24th Annual Conference on Engineering in Medicine and Biology 1971, Las Vegas, Nevada, vol. 13. Washington, D. C., The Alliance for Engineering in Medicine and Biology, Dennis H. LeCroissette, Chairman, p. 281.

Stinson, E.B., Rahmoeller, G.A., Tecklenberg, P.L., Colvin, S.B., Jones, K.W., and Pierce, J.E.: Left ventricular hemodynamic and dimensional responses to treadmill exercises in normal and cardiac denervated dogs. In Transactions of the National Conference on Research Animals in Medicine, Washington, D. C., 1972. (In press).

Wilson, S.H. and Kronick, M.N.: New assay technique for reactions that produce radioactive gases. Analytical Biochemistry, 43: 460-467, 1971.

Zaharko, D.S., Dedrick, R.L., and Oliverio, V.T.: Prediction of the distribution of MTX in the sting rays dasatidae sabina and sayi by use of a model developed in mice. Comparative Biochemistry and Physiology. (In press).

2. Patents

G.C. Riggle and J.P. White: Automated Device for Protecting Lens System. U. S. Patent No. 3,578,839, May 1971.

I. B. Tice, Jr.: Filter Circuit. U. S. Patent No. 3,566,291, February 1971.

III. INDIVIDUAL PROJECT REPORTS

Serial No. DRS-BEIB-1
1. Biomedical Engineering and Instrumentation Branch
2. Chemical Engineering Section
3. Bethesda

PHS-NIH
Individual Project Report
July 1, 1971, through June 30, 1972

Project Title: Pharmacokinetics

Previous Serial Number: DRS-BEIB-1

Principal Investigators: Robert L. Dedrick, Daniel S. Zaharko, Kenneth B. Bischoff

Other Investigators: Vincent T. Oliverio, Henry L. Gabelnick, Anthony M. Guarino, Donald D. Forrester, Robert J. Lutz

Cooperating Units: LCHPH-NCI, LT-NCI

Man Years:

Total:	3.0
Professional:	2.0
Other:	1.0

Project Description:

Objectives: To develop mathematical models for detailed distribution and disposition of drugs and environmental contaminants to provide an operational basis to:

(1) Account for species differences in drug distribution.

(2) Examine physical bases for extrapolation of toxicity from animals to man.

(3) In conjunction with cytokinetics, provide a basis for optimization of anti-cancer drug treatment.

(4) Permit more rational use of metabolic data determined *in vitro*.

Methods Employed: Mathematical models are developed which use physicochemical, physiological and anatomical information organized according to principles of chemical reaction engineering. Resulting sets of differential equations are solved analytically or numerically and compared with experimental data. Areas of uncertainty are clarified by additional experiments and model modification.

Major Findings:

(1) A mathematical model developed and verified for several mammalian species was successful in simulating the distribution of methotrexate in the sting ray.

(2) *In vitro* enzyme kinetics were successfully employed in conjunction with a compartmental model to predict plasma concentration of Ara-C and its major metabolite in patients.

(3) The role of hepatic blood flow in influencing ethanol metabolism *in vivo* was clarified.

(4) A cytokinetic model was used in connection with pharmacokinetics to simulate the behavior of L-1210 leukemia in mice.

Significance: Drugs and other chemicals are tested for toxicity in animals; the extrapolation of the results to predict risk in man is a subject of serious concern. At issue are both the risk associated with environmental contaminants and the optimal use of drugs in therapy.

Proposed Course : Continued strong emphasis on pharmacokinetic modeling with particular attention to incorporation of metabolic processes. Increased emphasis on biologic effects through both experimentation and use of cytokinetics in conjunction with pharmacokinetics.

Honors and Awards: Ebert Prize from Academy of Pharmaceutical Sciences to Dr. Bischoff for paper on "Methotrexate Pharmacokinetics," in *Journal of Pharmaceutical Sciences*, 60: 1128-1133, 1971, with Honorable Mention to coauthors, Dr. Dedrick, Dr. Zaharko, and Mr. Longstreth.

Publications:

Bischoff, K.B., Dedrick, R.L., Zaharko, D.S., and Longstreth, J.A.: Methotrexate pharmacokinetics. *Journal of Pharmaceutical Sciences*, 60: 1128-1133, 1971.

_____, Himmelstein, K.J., Dedrick, R.L., and Zaharko, D.S.: Pharmacokinetics and cell population growth models in cancer chemotherapy. *Advances in Chemistry Series*. (In press).

Dedrick, R.L. and Zaharko, D.S.: Letter to the editor - Extrapolation of teratogenic effects. *Chemical and Engineering News*, 5-6, May 17, 1971.

_____, Forrester, D.D., and Ho, D.H.W.: *In vitro* - *in vivo* correlation of drug metabolism - Deamination of 1-β-D-Arabinofuranosylcytosine. *Biochemical Pharmacology*, 21: 1-16, 1972.

Serial No. DRS-BEIB-2
1. Biomedical Engineering and
   Instrumentation Branch
2. Chemical Engineering Section
3. Bethesda

PHS-NIH
Individual Project Report
July 1, 1971, through June 30, 1972

Project Title: Development of Metal Complex Compounds for Control of Tumors

Previous Serial Number: None.

Principal Investigators: André F. LeRoy, Anthony Guarino

Other Investigators: None.

Cooperating Unit: LCP-NCI

Man Years:

Total:	1.0
Professional:	0.8
Other:	0.2

Project Description:

Objectives: Development and characterization of metal complex molecules with organic and inorganic ligands which exhibit significant biological effects. Synthesis and biological tests of platinum-metal complexes for anti-tumor activity.

Methods Employed: Apply established and innovative chemical synthesis methods when possible and devise new synthesis procedures when necessary for preparation of new compounds; use available physical chemical means for characterizing compounds prepared. Cell culture techniques and *in vivo* testing with mice and other animals.

Major Findings: Preparation of cis-diamminedichloropalladate, ammonium tetrachloropalladate and potassium tetrachloropalladate was accomplished. The first two effectively inhibit growth of L-1210 cells in culture.

Significance: Identification of metal complex molecules that effectively control tumor growth is significantly self-evident; investigation and characterization of such compounds can help to identify modes of action and suggest other potentially useful complexes.

Proposed Course: Enhance ability to synthesize and characterize complexes. Develop analytical methods for measurement, characterization and distribution of metal species in various organs of test animals.

Honors and Awards: None.

Publication:

LeRoy, A.F. and Morris, J.C.: The kinetics of hydrolysis of rutheniumnitrosyltrichloride. Journal of Inorganic and Nuclear Chemistry, 33: 3437-3453, 1971.

Serial No. DRS-BEIB-3
1. Biomedical Engineering and Instrumentation Branch
2. Chemical Engineering Section
3. Bethesda

PHS-NIH
Individual Project Report
July 1, 1971, through June 30, 1972

Project Title: Biomaterials

Previous Serial Number: DRS-BEIB-3

Principal Investigators: John W. Boretos, Henry L. Gabelnick

Other Investigators: Robert L. Dedrick, Robert J. Lutz, John I. Peterson

Cooperating Units: None.

Man Years:

Total:	1.0
Professional:	1.0
Other:	.0

Project Discription:

Objectives: To enhance understanding of properties of biomaterials with emphasis on the interaction of natural and synthetic materials with the physiological environment.

Methods Employed:

(1) Measurement of chemical and physical effects of long-term implantation.

(2) Development of new fabrication techniques for special purpose cannulas and other devices.

(3) Characterization of permeabilities.

Major Findings: None during this reporting period.

Significance: Physiologically compatible, stable materials with desirable physical properties are needed for many biomedical research and clinical applications. Characterization of desorption rates for additives from polymer systems and absorption of bodily constituents are important aspects in determining the utility of biomaterials.

Proposed Course:

(1) Detailed study of the kinetics and equilibrium distribution of absorbed and eluted components between polymers and a simulated physiological environment.

(2) Animal implant studies.

(3) Development of new techniques.

Honors and Awards: None.

Publications:

Boretos, J.W.: Biomedical materials compatibility and the design challenge. Paper 71-DE-8, American Society of Mechanical Engineers Design Engineering Conference and Show, New York, N. Y., April 19-22, 1971. ASME Headquarters, 345 East 47th Street, New York, N. Y. 10017.

_____: Communication to the editor - Tissue pathology and physical stability of a polyether elastomer on three-year implantation. Journal of Biomedical Materials Research. (In press).

_____: Long-term stability and compatibility of segmented polyurethane implants. In Proceedings of the 24th Annual Conference on Engineering in Medicine and Biology 1971, Las Vegas, Nevada, vol. 13. Washington, D. C., The Alliance for Engineering in Medicine and Biology, Dennis H. LeCroissette, Chairman, p. 212.

_____ and Wagner, F.R.: Communication to the editor: Particle fragmentation generated in pump sets. Journal of Biomedical Materials Research, 5: 411-412, 1971.

_____, Detmer, D.E., and Braunwald, N.S.: Factors influencing longevity of low-profile prosthetic heart valves. Journal of Biomedical Materials Research. (In press).

_____, _____, and Donachy, J.H.: Segmented polyurethane: A polyether polymer, II. Two years experience. Journal of Biomedical Materials Research, 5: 373-387, 1971.

_____, Bourke, R.S., Nelson, K.M., Naumann, R.A., and Ommaya, A.K.: Technique for unilateral isolation of the subdural space in the intact primate. Journal of Neurosurgery, xxxv: 101-107, 1971.

Detmer, D.E., McIntosh, C.L., Boretos, J.W., and Braunwald, N.S.: Polypropylene poppets for low-profile prosthetic heart valves. The Annals of Thoracic Surgery, 13: 122-127, 1972.

Gabelnick, H.L. and Litt, M. (Eds.): Rheology of Biological Systems. Springfield, Ill., Charles C. Thomas. (In press).

Serial No. DRS-BEIB-4
1. Biomedical Engineering and Instrumentation Branch
2. Chemical Engineering Section
3. Bethesda

PHS-NIH
Individual Project Report
July 1, 1971, through June 30, 1972

Project Title: Tumor Growth on Semipermeable Membranes

Previous Serial Number: None.

Principal Investigators: Richard A. Knazek, Pietro M. Gullino, Robert L. Dedrick, Robert J. Lutz

Other Investigator: William R. Kidwell

Cooperating Unit: LB-NCI (Project No. 5219)

Man Years:

Total:	1.3
Professional:	1.3
Other:	.0

Project Description:

Objectives:

(1) Development of effective devices and techniques for culture of solid tumors *in vitro* to study physiology, biochemistry and drug effects.

(2) Elucidation of transport mechanisms between tumors and implanted membrane cells in the study of metabolism and drug concentration *in vivo*.

Methods Employed: Devices have been developed composed of capillary membranes which are permeable to nutrients, metabolites, oxygen and carbon dioxide. Transport characteristics of these and other membrane devices have been evaluated *in vitro*. Tumor cells have been grown on the outside of capillary membranes perfused with oxygenated nutrient solution.

Major Findings: L-cells formed nodules 1-2 mm in diameter suggesting a release from contact inhibition. Human choriocardinoma also grew to multilayer depths.

Significance: It may be possible to grow cells *in vitro* to densities that approach those of solid organs or tumors. The resulting structures are expected to possess properties that differ from those of cells grown in monolayer culture. They may approach behavioral potential of the _in vivo_ state and permit study of metabolism and drug sensitivity. High cell densities could also be useful in production of large quantities of cellular products.

Proposed Course: Further investigation of transport characteristics and development of improved devices. Application of existing system to new cell lines.

Honors and Awards: Patent applied for on "Cell Culture on Hollow Fibers."

Publications: None.

Serial No. DRS-BEIB-5
1. Biomedical Engineering and Instrumentation Branch
2. Electrical and Electronic Engineering Section
3. Bethesda

PHS-NIH
Individual Project Report
July 1, 1971, through June 30, 1972

Project Title: Fluorometric Monitoring of Cortical Surface Metabolism

Previous Serial Number: None.

Principal Investigators: William H. Schuette, Michael J. O'Connor,
John M. Van Buren

Other Investigator: Darrell V. Lewis

Cooperative Unit: SN-NINDS (Project No. NDS I 54 SN-OC (C))

Man Years:
Total: 1.5
Professional: 1.0
Other: 0.5

Project Description:

Objectives: Innovate and implement instrumental systems to monitor metabolic activity on selected portions of exposed human cortex during surgery.

Methods Employed: Quantitative comparison of fluorescent light at 450 mμ with reflected light at 366 mμ from 366 mμ excited NADH in superficial cortical layers.

Major Findings: A prototype system has been successfully demonstrated using animals; a modified system is being evaluated for humans in the operating room environment; such measurements have not been feasible heretofore.

Significance: This nondestructive technique is expected to provide important new knowledge of energetic phenomena in the human brain.

Proposed Course: Improve utility and performance of current system with emphasis on sensitivity, precision, and ease of operation during surgery.

Honors and Awards: None.

Publications: None.

Serial No. DRS-BEIB-6
1. Biomedical Engineering and Instrumentation Branch
2. Electrical and Electronic Engineering Section
3. Bethesda

PHS-NIH
Individual Project Report
July 1, 1971, through June 30, 1972

Project Title: Nuclear Magnetic Resonance Techniques for Biochemical Analysis

Previous Serial Number: None.

Principal Investigators: Thomas R. Clem, Walter S. Friauf, Edwin D. Becker

Other Investigator: James A. Ferretti

Cooperating Units: LPB-NIAMD (Project No. 8)
PSL-DCRT (Project No. 5.11)

Man Years:

Total:	4.0
Professional:	3.0
Other:	1.0

Project Description:

Objectives: Innovate and implement improved methods for structural elucidation of organic molecules by means of nuclear magnetic resonance with emphasis on ^{13}C.

Methods Employed: Coherent pulse train excitation of samples in intense magnetic fields derived from super-conducting magnets with Fourier transformation of resonant response.

Major Findings: Operating experience demonstrates utility and flexibility using coherent generation of complex 55 MHz pulse trains.

Significance: Speed, sensitivity and precision of methods derived to date enable relaxation of sample stability criteria and facilitate heretofore unfeasible analyses of materials containing ^{13}C.

Proposed Course: Improve performance of current system with emphasis on heteronuclear decoupling, data acquisition and processing; extend techniques in terms of specificity and reliability.

Honors and Awards: None.

Publications: None.

Serial No. DRS-BEIB-7
1. Biomedical Engineering and Instrumentation Branch
2. Electrical and Electronic Engineering Section
3. Bethesda

PHS-NIH
Individual Project Report
July 1, 1971, through June 30, 1972

Project Title: Psychophysiological Conditioning via Aversive Stimulation

Previous Serial Number: None.

Principal Investigators: Walter S. Friauf, Glenn A. Rahmoeller, Theodore R. Tjossem

Other Investigator: William H. Schuette

Cooperating Unit: MR-NICHD (Project No. N-309769)

Man Years:

Total:	1.1
Professional:	0.7
Other:	0.4

Project Description:

Objective: Chronically curb self-destructive actions by autistic patients.

Methods Employed: A lightweight, wearable, helmet-mounted acceleration sensing apparatus and battery-powered electronic package delivers an audible tone and low level electrical shock to the upper arm when blows are delivered to the region of the head.

Major Findings: System has demonstrated effectiveness by almost completely eliminating self-destructive behavior patterns in one severe case; after a few months of conditioning, apparatus need not be used full time; reliability, portability, convenience and safety are adequate for chronic applications.

Significance: Substantial reduction and, potentially, complete elimination of self-destructive traits found in some autistic patients can be of immeasurable value to such patients and their families.

Proposed Course: Refinement of design of the apparatus and dissemination of information so as to encourage commercial development.

Honors and Awards: None.

Publications: None.

Serial No. DRS-BEIB-8
1. Biomedical Engineering and Instrumentation Branch
2. Electrical and Electronic Engineering Section
3. Bethesda

PHS-NIH
Individual Project Report
July 1, 1971, through June 30, 1972

Project Title: Ultrasonic Measurement of Cardiac Dynamics

Previous Serial Number: None.

Principal Investigators: Edward B. Stinson, Glenn A. Rahmoeller

Other Investigator: Paul Tecklenberg

Cooperating Unit: Surg-NHLI

Man Years:

Total:	1.2
Professional:	0.8
Other:	0.4

Project Description:

Objective: Innovate and implement improved methods for *in vivo* determination of cardiac geometries during exercise.

Methods Employed: Endocardially implanted piezoelectric transducers generate and respond to ultrasonic pulses in time intervals directly related to relative displacements.

Major Findings: Left ventricular diameters and endocardial surface velocities have been derived from travel times of an 8 MHz pulse between two transducers implanted in opposing positions of the endocardium of testing and exercising normal and chronically denervated dogs.

Significance: Effective measurement techniques for studying cardiac performance are crucial to progress in biomedical research.

Proposed Course: Enhance performance of current system with emphasis on refined transducer properties, investigation of more complex transducer arrays, and improvement of data acquisition and processing; extend techniques to human applications.

Honors and Awards: None.

Publication :

Stinson, E.B., Rahmoeller, G.A., Tecklenberg, P.L., Colvin, S.B., Jones, K.W., Pierce, J.E.: Left ventricular hemodynamic and dimensional responses to treadmill exercises in normal and cardiac denervated dogs. In Transactions of the National Conference on Research Animals in Medicine, Washington, D. C., 1972. (In press).

Serial No. DRS-BEIB-9
1. Biomedical Engineering and Instrumentation Branch
2. Electrical and Electronic Engineering Section
3. Bethesda

PHS-NIH
Individual Project Report
July 1, 1971, through June 30, 1972

Project Title: Viable Cell and Neuron Activity Monitoring in Tissue Culture

Previous Serial Number: None.

Principal Investigators: Edward J. Thompson, Jimmy M. Griffith

Other Investigator: Marshall Nirenberg

Cooperating Unit: LBG-NHLI

Man Years:

Total:	1.2
Professional:	0.8
Other:	0.4

Project Description:

Objective: Quantitatively detect and record action potentials from cells and neurons in tissue culture with minimal disturbance to preparations.

Methods Employed: Conventional intracellular recording was excessively traumatic. Extracellular recording with microelectrodes gave poor signal to noise ratio and still caused excessive disturbance because of electrolyte leakage. Therefore metal electrodes and large bore micropipettes filled with tissue culture medium were finally utilized.

Major Findings: It was found that both the latter types of electrodes were satisfactory from the standpoint of not disturbing the environment, and that by making the tip much larger than usual, greatly improved signal to noise ratio could be obtained.

Significance: Effective monitoring of single cells and neurons in tissue culture will provide important scientific insight into neurophysiological phenomena.

Proposed Course: Refine instrumental techniques and extend investigation to definition of and communication within neuronal networks.

Honors and Awards: None.

Publications: None.

Serial No. DRS-BEIB-10
1. Biomedical Engineering and
   Instrumentation Branch
2. Mechanical Engineering Section
3. Bethesda

PHS-NIH
Individual Project Report
July 1, 1971, through June 30, 1972

Project Title: Atraumatic Electrical Sensing in Brain Cortex

Previous Serial Number: None.

Principal Investigator: Seth R. Goldstein

Other Investigator: Michael Salcman

Cooperating Unit: LNC-NINDS

Man Years:

Total:	1.4
Professional:	1.0
Other:	0.4

Project Description:

Objective: Achieve stable electrode location and reliable acute recording of brain cell activity beneath the pulsating cortex at prescribed depths up to one cm with minimum tissue damage.

Method Employed: A conducting wire electrode is advanced by a fine lead screw within a frictionless pneumatically balanced piston-cylinder retainer that "floats" on the cortical surface and automatically compensates for axial and lateral pulsations.

Major Findings: Evaluation of technical design and prototype models assure feasibility; working instrument is in construction.

Significance: Depth recording of CNS cell activity in humans has been limited because of difficulty in achieving atraumatic intervention. These new methods, if successful, are expected to enable a considerable increase in acquisition of information necessary to enhance understanding of brain function.

Proposed Course: Refinement of techniques and apparatus, testing and evaluation with animals and humans and clinical applications; enlargement of device family for related types of measurement requirements.

Honors and Awards: None.

Publications: None.

Serial No. DRS-BEIB-11
1. Biomedical Engineering and Instrumentation Branch
2. Mechanical Engineering Section
3. Bethesda

PHS-NIH
Individual Project Report
July 1, 1971, through June 30, 1972

Project Title: Biomechanical Concomitants of Head Injury

Previous Serial Number: None.

Principal Investigators: Lawrence E. Thibault, Ayub K. Ommaya, Thomas A. Gennarelli

Other Investigators: Stephen B. Leighton, Howard D. Metz

Cooperating Unit: SN-NINDS

Man Years:

Total:	3.0
Professional:	1.7
Other:	1.3

Project Description:

Objectives: Define rheological properties of brain tissue, especially as related to severe mechanical stress; establish rational criteria for determining injury thresholds and traumatic unconsciousness.

Methods Employed: Mathematical analysis of mechanical phenomena; experimentation with animals and analog models.

Major Findings: Revisions of conventional analytical approaches and experimental designs produce considerable new insight into fundamental processes.

Significance: A rationally derived basis for understanding the phenomena of unconsciousness and brain damage because of mechanical head injury is an issue of key importance in medical diagnosis, therapy, and accident amelioration.

Proposed Course: Critical review of previous work, development of improved experimental designs and apparatus, synthesis of effective analytical and simulation models at microscopic and macroscopic levels.

Honors and Awards : None.

Publications:

Gennarelli, T.A., Thibault, L.E., Ommaya, A.K.: Comparison of translational and rotational head motions in experimental cerebral concussion. In Proceedings of Fifteenth Stapp Conference, November 1971, San Diego, Cal. (In press).

Metz, H., McElhaney, J., and Ommaya, A.K.: A comparison of the elasticity of live, dead, and fixed brain tissue. Journal of Biomechanics, 3: 453-458, 1970.

Serial No. DRS-BEIB-12
1. Biomedical Engineering and Instrumentation Branch
2. Office of the Chief
3. Bethesda

PHS-NIH
Individual Project Report
July 1, 1971, through June 30, 1972

Project Title: Autologous Blood Reinfusion

Previous Serial Number: None.

Principal Investigators: Grant C. Riggle, Robert C. Hoye

Other Investigator: Stephen H. Bennett

Cooperating Unit: Surg-NCI (Project No. NCI-3806)

Man Years:

Total:	1.0
Professional:	1.0
Other:	.0

Objectives: Safely collect and reinfuse patients' blood released by surgical procedures or accidentally-caused hemorrhage.

Methods Employed: Aspirate blood pools in body cavities, introduce anticoagulant at entrance to an extracorporeal pump, introduce precisely regulated amounts of coagulant at pump exit prior to bodily reentry.

Major Findings: Prototype apparatus successfully demonstrated with animals; preliminary clinical evaluation with humans is encouraging.

Significance: Effective means for reinfusing autologous blood should substantially enhance patients' recovery, reduce dependence on alien donor sources and minimize potential hazards of incompatible or infectious agents.

Proposed Course: Continued improvement of instrumentation to meet operating room specifications. Eventual utilization of complete system for recovery and reinfusion.

Honors and Awards: Patent application filed.

Publications:

Bennett, S.H., Hoye, R.C., and Riggle, G.C.: Intraoperative autotransfusion. The American Journal of Surgery, 123: 257-260, 1972.

Riggle, G.C., Hoye, R.C., and Bennett, S.H.: An autologous blood reinfusion device - preliminary report. In Proceedings of the 24th Annual Conference on Engineering in Medicine and Biology 1971, Las Vegas, Nevada, vol. 13. Washington, D. C., The Alliance for Engineering in Medicine and Biology, Dennis H. LeCroissette, Chairman, p. 281.

Serial No. DRS-BEIB-13
1. Biomedical Engineering and Instrumentation Branch
2. Office of the Chief
3. Bethesda

PHS-NIH
Individual Project Report
July 1, 1971, through June 30, 1972

Project Title: Automated Precision Fluorometry

Previous Serial Number: None.

Principal Investigator: John I. Peterson

Other Investigators: Walter S. Friauf, Stephen B. Leighton, Richard L. Veech

Cooperating Unit: SMR DN, IRP, MH

Man Years:

Total:	2.0
Professional:	1.5
Other:	0.5

Project Description:

Objectives: Produce an instrumentation system to detect subtle changes in metabolic activity of physiological cell types as manifested by variations of fluorescent reactions.

Methods Employed: Measurements of fluorescent light are made on a sequence of 20 biological sample solutions both before and at prescribed time intervals after pre- and post-injection of an activating reagent. Pre- and post-injection light readings are compared to yield quantitative assays of enzyme substrates.

Major Findings: System successfully demonstrates ability to produce precise readings of fluorescent light differentials to within one part in 100 in circumstances where ratio of inherent background fluorescent to signal fluorescence is on the order of 100 to one. Automatic sample and data processing are necessary to achieve desired results.

Significance: Substantial benefits to research on cellular metabolism should be derived by availability of this technique which enables unprecedented sensitivity, reliability, and convenience of enzyme substrate analysis.

Proposed Course: Thorough testing and evaluation with a variety of tissue sample solutions and enzymes; refinement of methods as necessary; dissemination of information to public to encourage commercial production and distribution to the community.

Honors and Awards: Patent application submitted.

Publications:

Peterson, J.I.: Presentation of talk at 162nd National Meeting, American Chemical Society, Washington, D. C., September 17, 1971: "Design of a High Precision Fluorometer for Biochemical Measurement."

_____, Friauf, W.S., and Leighton, S.B.: A high precision fluorometer for measuring enzymatic substrates in tissue. In Proceedings of the 24th Annual Conference on Engineering in Medicine and Biology 1971, Las Vegas, Nevada, vol. 13. Washington, D. C., The Alliance for Engineering in Medicine and Biology, Dennis H. LeCroissette, Chairman, p. 164.

DIVISION OF RESEARCH SERVICES

Summary of Branch Activities July 1, 1971, through June 30, 1972

ENVIRONMENTAL SERVICES BRANCH Vinson R. Oviatt, Chief

I. SUMMARY

The Environmental Services Branch experienced an increased demand for environmental services during the year. This demand in conjunction with current economy measures was of such magnitude that the routine environmental surveillance programs were all but abandoned. Three factors explain the current situation. They are: (1) new standards of acceptability for the working environment as reflected by recent employee health and safety legislation and by increasing interest, sophistication and activity of employees and employee groups; (2) decreasing tolerance for adverse effects on the community environment reflected in local and national pollution control legislation; and (3) more stringent requirements for laboratory environmental control to match increasing subtleties and complexities of research. A review of the Branch program reflects these factors.

The Biological Control program received priority emphasis. A major portion of staff time was spent in consultation with NIH research personnel in assessing potential biological hazard problems and equipment use and procurement. The ad hoc Inter-Institute Technical Committee on Biohazards completed its mission and submitted a final report to the Deputy Director for Science. The Branch Chief served as secretary of the ad hoc committee and will continue to serve the permanent committee in the same capacity. The committee recommendations emphasize and add to the ESB program commitment. As a part of the committee activities, ESB developed a computerized registry of microbial agents, tissue cultures, and animals maintained at the NIH. This registry provides invaluable biohazard surveillance information. A contract was awarded to the Dow Chemical Company for testing and maintenance of Biological Safety cabinets, high efficiency filters and certain other biocontrol systems. Another contract effort resulted in the development and delivery of a laminar down flow biological hood for the handling of large containers of tissue cultures.

A modest effort was instituted in the surveillance of the use of highly toxic chemicals (carcinogens). Assistance was offered selected laboratories in their proper handling, storage and disposal of waste materials. A study of herbicide and insecticide residues in fresh water fish as possible causes of neo-plastic tumors was continued in cooperation with NCI and the Smithsonian Institute.

Water pollution control activities were stepped up at both the NIH reservation and at NIHAC. At the NIHAC, early efforts involved satisfactory operation of the "old" lagoon-spray field system. During the course of the year, the new water pollution control facility was constructed and staff assisted in start-up procedures and training of the operational staff in plant operation and laboratory methodology. Concurrent studies in water pollution control involved methodology for reclaiming mercury from liquids and the microbiological quality of surface waters.

The incinerator and boiler stacks were checked periodically for excess smoke, dust, fly ash, sulphur dioxide, and other gaseous contaminants for compliance with air pollution codes. A model study related to hood exhaust fume re-entry in the planned NIEHS North Carolina facility, building air supply system, was completed for OES. A second model study was completed of the Building 37 air intake system. The latter study provided recommendations for engineering solutions to the contamination of the building supply air by vehicles at the loading dock.

The handling and disposition of solid waste at NIH consumed a major portion of staff time during the months of December, January, and February. Construction of the Tri-Service Incinerator was suspended in December pending submission of an Environmental Impact Statement ordered by the Court. ESB reviewed in depth the many draft statements prepared by FECA and provided suggested revisions for portions of the final statement. These involved air pollution parameters, waste handling procedures, and transportation of materials from NIH grounds to the Tri-Service site. Earlier in the year, the waste transition study started in FY 1971 was completed.

ESB assumed total responsibility for the surveillance of the Clinical Center environment due to the phaseout of DESC, CC. Staff involvement included assessing problems in the laundry concerning unnecessary exposure of personnel and clean work to potential contamination; design participation and planning for the NICHD Reproductive and Perinatal Biology facility and improvements to the NCI chemotherapy patient protected environment facility; and assistance in a program for disposal of used needles and syringes in patient areas. Two major studies were conducted to assist the hospital in the provision of increased patient care and protection. They were a microbiological evaluation of the cidamatic decontamination system for washing and disinfecting gas anesthesia circuits for the anesthesiology department and development of a prototype laminar flow air system for the neuro-surgical operating rooms in cooperation with the Surgical Neurology Department, NINDS, and the Engineering Design Branch, OES.

ESB activities constitute a direct contribution to the NIH program for improvement of human relations. The ESB is a member of the Environmental Differential Pay Committee which investigates working conditions warranting extra pay. ESB originated some of the items in the NIH program for correcting environmental deficiencies for lower pay level employees, and participated in the investigation and evaluation of most of the items. Within ESB, a monthly meeting of the entire staff to cultivate employee-management rapport includes opportunities for a report and discussion of DRS, EEO activities, and an airing of problems or questions raised by any Branch member. A system of employee appraisal of all supervisors, developed by ESB during the DRS Human Relations Seminar, was put to use in the 1972 employee performance review.

[illegible] LIBRARY

II. BRANCH PROGRAMS

A. Objective

The Environmental Services Branch objectives at NIH and its field stations are:

1. To locate and solve environmental problems.

2. To provide a safe, compatible environment for patients, staff, and the surrounding community.

3. To promote an environment conducive to a quality research program.

B. Current Programs

Attainment of the Branch objectives was approached through the following closely coordinated program areas.

1. Biohazards and Contamination Control

The biohazards and contamination control program is aimed towards promoting a safe environment for personnel and protection to research work at all NIH facilities in Bethesda and in the field. The basic approaches followed in dealing with potentially hazardous laboratory and animal room areas are regular surveillance of Institute programs, control equipment, and facilities; and development on a case-by-case basis of laboratory arrangements needed to protect the investigator and the public.

2. Industrial Hygiene

The industrial hygiene program is devoted to the recognition, evaluation, and control of environmental factors or stresses which may cause sickness, impaired health and well-being or significant discomfort among workers or citizens of the community. Major workload is related to both gaseous and particulate air contamination (including air pollution) potentially or actually generated at NIH. Problems connected with noise, temperature extremes, and non-ionizing radiation are also part of this program.

3. Hospital Sanitation

The hospital sanitation program in the Clinical Center is aimed at the protection of patients from environmental influences which could contribute to nosocomial disease. It encompasses the regular visual and microbial surveillance of patient treatment and care areas as well as relevant support departments.

4. General Sanitation and Sanitary Engineering

The general sanitation and sanitary engineering program is concerned with basic environmental factors which affect the health of NIH employees, visitors and the quality of the research environment. These factors include the food sanitation, water supply, solid and liquid waste disposal, housekeeping practices, pesticides, and water pollution control.

5. Environmental Studies for Support of Research and Patient Care

Continuing environmental studies are conducted as a necessary adjunct to surveillance and consultation activities. Studies are oriented to environmental systems and problems; evaluation of new equipment and methods; provision of quality glassware, animals, and water; environmental stresses related to light, heat, noise, food, water, and waste; and the identification of environmental contaminants.

6. Training

Training is provided for the benefit of both ESB personnel and staff members at NIH. All professional and technical staff of ESB attend relevant short courses and/or formal academic programs. Environmental control devices and practices related to the general research environment require special training for proper operation and handling. Therefore, ESB personnel conduct continuing programs for NIH employees in a variety of problem areas.

C. Program Progress and Accomplishments

1. Biological Control

The ad hoc Inter-Institute Technical Committee on Biohazards has completed its mission and submitted the final report to the Deputy Director for Science. The recommendations of the committee provide for the establishment of a NIH-wide biohazard program consisting of the following components:

a. Establishment of a standing NIH Biohazard Committee.

b. A central registry of biological materials.

c. Provision of environmental consultation and services.

d. An expanded medical surveillance program.

e. Training in biohazard control and laboratory safety.

f. Research and development of environmental controls.

g. Handling of feral animals.

These recommendations are of great import to ESB as they formalize and give direction to the Biological Control Program. The Chief of ESB will serve as secretary of the standing committee. ESB is also responsible for the central registry of biological materials, provision of environmental consultation and services, training programs and R & D of environmental controls. The registry of microbial agents, tissue cultures and animals maintained at the NIH was prepared by ESB during the year from information furnished by investigators. The computerized system permits retrieval of such information as the types of agents handled in a certain building by a specific investigator or by degree of hazard. The program is designed to enable ESB to work more efficiently in management of biohazards.

The Dow Chemical Company was awarded a contract, NIH-72-C-7-CC, for testing and maintenance of biological safety cabinets (hoods), high efficiency filters, and certain other biocontrol systems. Safety clearance or the need for decontamination of systems is determined by ESB prior to testing. Over 85 laminar flow hoods have been tested since the contract was initiated in late February. This program represents one of the basic essentials for biohazards control.

Specifications were developed for a decontamination chamber to be located on the third floor of building 13. The facility will be used to decontaminate equipment undergoing repairs or to be surplused. ESB is collaborating with OES on design requirements.

A major portion of staff time was spent in consultation with NIH research personnel in assessing potential biological hazard problems and equipment use and procurement. Decontamination services were provided for animal infection outbreaks and procedural recommendations made for contamination control. Research laboratories labeled with the biohazard symbol as outlined in PPM #16 were updated with 36 currently posted. Requests for biological control procedures from private research institutions and other governmental agencies showed a marked increase over the past year. Meetings were held with equipment manufacturers interested in meeting NIH requirements for biohazard control.

A visit was made to the Middle America Research Unit in Panama to decontaminate the building exhaust filters of the high hazard suite for replacement with new HEPA filters. In addition to testing the newly installed filters for leaks, other biosafety checks were made. Decontamination and testing of new filters in the air exhaust system of Building 36, 5-C isolation suite, was completed. Decontamination and testing of the house vacuum system in Building 41; review of new construction and alterations to isolation suites; approval of ultraviolet light installations are representative of services provided.

2. Industrial Hygiene

Major activities were oriented towards surveillance of air pollution sources, stack testing, and consultations in specific areas. Most of the consultations related to material toxicity, procedures and equipment needed for the safe handling, and proper disposal techniques to be employed. Problems related to hot environments and noise were also evaluated. The routine chemical hood surveillance for the nearly 800 hoods at NIH was continued during the year.

The renovation of Building 6 was completed. ESB staff was involved in problems associated with specifications, acceptance tests, and building and equipment evaluations.

3. Hospital Sanitation

During the year, ESB assumed total responsibility for the surveillance of the Clinical Center environment due to the phase-out of DESC, CC. A protocol detailing ESB services to the CC was prepared and submitted to the Clinical Center management as part of the assumption of services.

As service elements in the ongoing hospital program, significant amounts of staff time were devoted to regular surveillance and responding to requests for problem solving assistance. Typical of these functions were: evaluating and recommending changes in structure, air control, and material flow patterns in the surgical suite at Saint Elizabeths Hospital, NIMH; maintaining high frequency laboratory surveillance of dairy products supplied to the Clinical Center in order to resolve persistently recurrent problems with sub-standard microbial quality; assessing problems in the Clinical Center Laundry concerning the unnecessary exposure of personnel and clean work to potential contamination from soiled fabrics; actively participating in design deliberations and recommending changes in order to avoid environmental problems with such major Clinical Center construction projects and system improvements as the NCI Chemotherapy Program's patient protected environment facility in the 2-B south wing, the NICHD proposed three-floor addition to the D-wing for a Reproductive and Perinatal Biology Facility, and the upgrading of the air handling system serving the south side of Building 10; in cooperation with the Safety and Fire Prevention Branch, ODA, studying safety, infections and security problems associated with the use of needles and syringes in patient areas; and recommending procedural changes to solve the contamination problems relating to the processing of blood and blood fractions in the Clinical Center Blood Bank.

4. General Sanitation and Sanitary Engineering

ESB expended major effort in preparation of Environmental Impact Statements in conjunction with OES for the Tri-Service Incinerator, NIH Master Plan, and the NIEHS North Carolina Research Facility. The Tri-Service Incinerator project was the most involved and time-consuming effort. This was the result of a court order suspending construction on the Incinerator pending submission of an Environmental Impact Statement. ESB reviewed, in depth, the draft statements prepared by FECA and provided suggested revisions for portions of the statement.

Water pollution control was also a foremost activity. Of major concern is the disposal of liquid waste at NIHAC. Preparation of informational material on the operation of the lagoon-spray field was prepared for Congressman Gilbert Gude, Maryland. During the summer months, ESB stepped up activities in conjunction with OES to ameliorate odor and drainage problems at the lagoons and spray field. Late in the year, the new water pollution control plant was completed at the NIHAC with ESB staff intensively involved with the training, monitoring and consultations dealing with the start-up problems of the new facility. Stream pollution control efforts were also expended at the NIH campus. The major contaminate of the NIH stream has been vehicle washings which drained to the stream. Staff efforts have resulted in OES designing a vehicle wash facility which will be constructed during the coming fiscal year. The facility will reduce but not eliminate all water pollution problems on the reservation. Due to fund limitations it will be minimal in nature.

The program to eliminate mercury as an environmental pollutant at NIH continued. ESB established a monitoring program and in cooperation with OES developed traps for collection of mercury in the NIH sanitary sewers. In addition, in cooperation with the Plant Safety Branch, ODA, a manual issuance was prepared to outline proper recycling and disposal procedures for mercury and products and solutions containing mercury.

Provision of high purity water for NIH research needs was a continuing high priority program. Regular monitoring procedures assisted in managing the program. Five hundred and fifteen samples of distilled and deionized water were analyzed. Many problems were encountered in newly installed systems.

Environmental and food sanitation problems were numerous. In general, there was no overall improvement of conditions from the previous year. The lack of adequate, properly trained, personnel is directly or indirectly responsible for the problem situations which are of concern in the food service areas and with general sanitation of buildings and grounds. Weekly laboratory analysis of dairy products became necessary because of poor quality control at the only dairy product supplier to NIH.

5. Environmental Studies

The staff was involved in several studies, many of inter-disciplinary nature, to meet the varied needs and problems at NIH. Selected examples are:

a. A laminar downflow biological hood was modified for handling large containers of up to five gallons of tissue cultures. The hood incorporates an adjustable vertical work surface, has front access for safe loading and unloading and a power driven "elevator" platform will raise the container so that the mouth is at the critical face opening of the work surface. The hood was developed under contract. Several researchers have indicated an interest in use of such a hood.

b. A substantial effort is underway to devise a satisfactory solution to problems arising from the design and operation of the air handling systems serving the neurosurgical operating rooms. Under present circumstances, it is necessary to introduce clean supply air directly over the operating table sites at an undesirably low temperature in order to maintain necessary air flow patterns, from the air hygiene viewpoint. This results in excessive chilling of both patients and personnel with a consequent body temperature loss to patients of several degrees, during protracted procedures under general anaesthetic. In order to eliminate the problem and still maintain required air flow patterns, ESB has advocated the design and installation of a clean air flushing (laminar) system. ESB has designed and had fabricated, under private contract, a prototype module for demonstration and study purposes which has resulted in the identification of noise generation as the principal obstacle to final design and installation. This project is being worked on cooperatively with personnel from the Surgical Neurology Branch, NINDS, and the Engineering Design Branch, OES.

c. A study was completed relating to probability of hood exhaust fume re-entry in the planned NIEHS North Carolina facility building supply air system. The results obtained in the tests indicated the pollution potential under various wind conditions and exhaust stack configurations and confirmed the wisdom of a changed stack discharge configuration which has been adopted.

d. The Building 37 scale model smoke test studies started last year were completed and a report submitted recommending that one of several engineering solutions be adopted. The problem relates to contamination of the building supply air by vehicles at the loading dock. Although no corrective changes have yet been made, a preliminary design study has been completed; and a final design will be funded this year. Complaints this year have been fewer due to better cooperation of personnel at the loading dock.

e. A study of herbicide and insecticide residues in fresh water fish as possible causes of neoplastic tumors was started. This project will be continued and expanded to include polychlorinated biphenyls and other compounds used in the environment.

f. A practical method for concentrating mercury residues in fluids was developed and is being used by the Plant Safety Branch. A method of analysis of liquid wastes for mercury content has also been developed and is sensitive and accurate at the 1.0 part per billion level.

g. Two pieces of laboratory equipment were developed and submitted to the NIH legal department for consideration for patent. They were the "Karamian Separatory Funnel" and "Mercury Reaction Vessel for Coleman Mercury Analyzer Model MAS-50."

h. A new technique for isolating Serratia marcesens from sewage samples has been developed.

i. High purity water piping systems have been found by ESB to contribute to contamination of the water. Samples of high purity Teflon tubing, coated with Fiberglass, are being tested to ascertain if the material is a suitable replacement for the currently used alumimum or tin lined pipe.

j. Regular monthly bacterial examination of animal feed and bedding products was provided VRB, DRS. The counts vary considerably but no indication of heavy pathogenic contamination has been noted to date.

k. A study of Serratia marcesens from various sources was carried on throughout the year. Most streams in the metropolitan area carried the organism. The use of a new media simplified the procedure to the use of a single plate. Two strains were isolated that almost resembled Serratia marcescens but when submitted to CDC for verification they were identified as Bacterium rubidaeum and were thus reported in this area for the first time.

l. A continuing study of disinfection problems is being carried on with preliminary studies indicating that disinfectants are being used indiscriminately with little or no effect.

m. A microbiological evaluation of the effectiveness of a cidematic decontamination system, in washing and disinfecting gas anaesthesia circuits was performed for the Anaesthesiology Department of the Clinical Center. Sixty-four units, including breathing hoses and rebreathing bags sampled, demonstrated a high level of effectiveness in disinfection of this equipment.

n. The Branch is collaborating with BEIB in the development of a plastic isolator enclosure for a centrifuge. BEIB is doing the design work and ESB is consulting on the decontamination system and testing of the unit.

6. Training

The training program offered by the Branch to other NIH employees was drastically curtailed during the year. This reduction was related directly to reduced staff and the loss of the Branch training officer.

ESB cooperated with the Veterinary Resources Branch, DRS, in provision of routinely scheduled animal caretaker training programs for NIH personnel.

The annual training program for NIH staff involved in insect and rodent control was provided. In lieu of an intensive course, a shortened format was provided to update personnel on current practices and materials.

Branch staff assisted in training the operators of the new NIHAC water pollution control treatment facility. The training included two weeks in laboratory methods associated with plant operation and stream pollution control.

The former one-hour training program on safety pipetting and the proper use of laminar downflow hoods has been enlarged to five two-hour sessions. These cover such additional topics as the proper care and control of inoculated animals, principles of disinfection and general laboratory procedures (waste disposal, clothing use). The extended course was presented to 18 laboratory technicians.

Established training instruction was continued in monthly orientation of new professional nurses in hospital environmental control and semi-annual orientation of para-professional nursing personnel.

A new training course was initiated on the "Role of Laundry Personnel in the Control of Contamination and Infections in Hospitals."

The hospital sanitarian presented lectures on hospital environmental control in a course approved by the Center for Disease Control aimed toward health care facilities.

The orientation instruction for NIH service personnel about the labeling program for biohazards in research facilities was continued. Approximately 80 personnel of BEIB,DRS, and the guard force received the instruction.

During the summer months, ESB provided laboratory and field experience in environmental health to a summer aid, a high ability high school student under the auspices of the National Science Foundation, to a high school chemistry teacher under the auspices of the National Science Foundation, and to a CO-STEP from Montana State University.

ESB personnel received 735 hours of training at designated short courses or in classroom experience at local community colleges and universities. ESB seminars were continued to provide "state-of-the-art" information to ESB staff and other interested personnel.

D. Problems

The manpower reduction and grade deescalation programs have necessitated abandonment for all practical purposes of the planned routine environmental surveillance program of the Branch. Three highly qualified staff members were lost because of inability to promote them to higher grades. The Branch is essentially reacting to immediate problems and the solution of individual situations. This is evident in review of Section C of this report indicating a decrease of activities in the industrial hygiene and training programs. Biological and pollution control activities are being supported at the expense of other programs.

An improved administrative mechanism must evolve for the reception and implementation of environmental needs expressed by ESB and other NIH organizations. As an example, three critical situations have been reported for at least two years without any corrective action. The three situations are: correction of the Building 10 water supply system to assure a safe supply; provision of an approved chemical waste disposal facility; and provision of an adequate air supply system for Building 10 to correct serious negative air pressure problems.

Quality control testing of new biological hood designs involving "Low Bidders" is required to verify containment performance. ESB has neither the staff nor the facilities to perform these tests and there is no known private laboratory approved to do this work. The possibility exists that it will be necessary to accept such equipment on a design basis only, thus allowing an influx of unknown or inadequate biological containment devices into NIH laboratories.

The provision of high purity water to NIH laboratories continues to be a problem. As in previous years, inappropriate amounts of time have been expended in solving problems of delivery of distilled and deionized water. A developmental contract to provide a series of solutions to these problems was negotiated during the last months of the fiscal year.

During the past two years, there has been a noticeable deterioration of quality or degree of cleanliness in offices, laboratories, and support areas of NIH. This conclusion is based on routine observation of staff and reports of concerned NIH employees. Predominant exceptions to the problem are Buildings 1, 31, and 10. Poor sanitation and litter can effect the research work, attitude and safety of the employees and present an intolerable image to visitors. Reasons given for these conditions are a lack of service employees in Housekeeping and Buildings and Grounds work groups.

Poor construction practices in laboratories continue to occur, particularly those in improper ceiling pipe chases and other service penetrations in walls and ceilings. Revision of outdated standard architectural and construction details used for laboratory construction need to be made. Penetration seals must be insect tight for laboratory facilities and gas tight for high hazard biological work.

E. Program Plans

Several measures will be taken to partially offset problems caused by staff reduction and grade deescalation. The ESB staff will be restructured to place major effort in the Biological and Pollution Control Programs. Existing and future vacancies in the Office of the Chief and the Laboratory Section will not be filled during FY 1973 in order to exert major effort in the field programs.

Automated sampling techniques are to be instituted for monitoring of air and water. Information on air quality at NIH will be regularly obtained from the state of Maryland automated sampler located at NIH. Data from this source will be substituted for ESB's generated information on air pollution with present air monitoring equipment to be used only for special studies. Automatic samplers are to be installed on Broad Run at the NIHAC to monitor water quality above and below the point of discharge of the new water pollution control plant. The computerized registry of biological agents will be used to direct major effort towards surveillance of laboratories in Building 10 where potential biohazards to patients, visitors, and employees may exist. Other areas of NIH will be surveyed on a priority basis from the registry, according to the level of hazard risk. The ESB planning mechanism is being reoriented to permit the use of computerized simulation techniques. It is hoped that such a program will assist in prediction of program needs and efficient utilization of available manpower.

Efforts will be directed to utilization of the coordinating safety council for the resolution and implementation of environmental programs and projects. The ESB will further stress needed corrective actions to the Deputy Director for Science through the Office of the Director, DRS.

A search will be made to identify a contractor with the capability to performance test biological containment equipment for procurement acceptance. If such efforts are not fruitful, effort will be made to stimulate formation of such a commercial laboratory. If such facilities can be identified, equipment will be submitted to the laboratory on a contract basis for biological testing.

ESB will make an effort to document problem areas regarding sanitation of offices, laboratories, and support areas. Upon identification of the areas, operational and cleaning procedures will be reviewed and assistance given to NIH housekeeping in training employees in an attempt to make them more productive and produce a higher quality environment.

The computer program for agent registration will be rewritten by DCRT this fall. The new program will include input from the Employee Health Service, CC. A changeover to conversational programming system (CPS) will probably be made to lessen the chance of error in feeding in information and provide for an overall more simplified retrieval.

The hospital sanitarian will serve as liaison for all environmental health work performed in Building 10. This is a departure from his previous responsibility only to patient care units and ancillary hospital departments.

Carcinogens are used in research at NIH in varying quantities and with widely varying procedures. An increased effort will be made to locate these materials, evaluate the conditions of their use, and make recommendations for appropriate control measures.

More frequent visits to the Rocky Mountain Laboratory will be planned. This should be coordinated with OES toward a long-range plan of improvement.

The course, "Biological Laboratory Safety," will be offered with a minimum of four times during FY 72-73.

A greater effort will be given to identifying operations in biohazards and hospital sanitation where uniform standards of operation should be developed. As part of this effort, the dissemination of information issuances will be on a more frequent basis.

F. Publications

Oviatt, V.R.: Summary of Discussion Control of Microbial Contamination. *Proceedings International Conference on Nosocomial Infections*. 246, 1971.

Herman, L.G. and Hart, L.J.: Role of Environmental Sampling. *Proceedings International Conference on Nosocomial Infections*. 268, 269 1971.

Morrison, R.P. and Oviatt, V.R.: Environmental Control Programs in Health Care Facilities. *Hospital Progress*. 52:96-108, 1971.

Morrison, R.P. and Oviatt, V.R.: Air Control in Hospitals. *The Bulletin of the Guthrie Clinic*. 42:62-72, 1971.

Ament, R.K.: A Study of Automatic Detergent Dispensers. *Laboratory Animal Care*. 21:984-989, 1971

Karamian, N.A.: Ventilation of Electron Capture Detectors. *Health Physics Journal*. In publication.

NIH LIBRARY

DIVISION OF RESEARCH SERVICES

Summary of Branch Activities July 1, 1971, through June 30, 1972

LIBRARY BRANCH Seymour I. Taine, Chief

I. SUMMARY

Some significant organizational and personnel changes have been beneficial for Library operations. A reception area and a consulting room were provided for the new Library Services Adviser program. New doors were made to give necessary access from section offices to working areas. Small tables and additional chairs were obtained for individual research in the Upper Level Reading Room.

The Library Advisory Committee continued to assist and support the program of the NIH Library. Dr. John S. Finlayson, DBS, was appointed Chairman in February, replacing Dr. Hewitt G. Fletcher who had served in that capacity for several years. At the same time, Institute/Division representatives were appointed to the Committee, adding six new members.

The U. S. Court of Claims ruled against the Government in the Williams and Wilkins case relating to the photocopy service and the copyright law. The Department of Justice will prepare briefs to be presented to the full Court of Claims.

The Library's electronic 3M TATTLE-TAPE Security System has been an asset in preventing unauthorized removal of Library books and journals both by NIH and non-NIH users.

Three Library Consultants to the NIH Library were appointed to advise the Branch Chief in the areas of automation and training for the professional staff.

Bibliographic searching is now conducted through National Library of Medicine's new MEDLINE computer system as well as through its MEDLARS system which has been in use for some years.

As a result of two feasibility studies relating to Acquisition activities, DCRT's WYLBUR system continues in use for monograph order procedures, and the PHILSOM system designed by Washington University School of Medicine Library was adapted for the journal control procedures.

The FY 1972 Branch Training Program was designed to meet the needs of all Library employees and was developed last year on a group basis.

Two trainee slots were established for the year to provide development of one GS 7/9 Library Technician and several GS 1-4 personnel to a higher level of duty performance. A course covering all aspects of library science designed particularly for Library Technicians was conducted each semester for GS 5-6 staff members by a faculty member of the University of Maryland School of Library and Information Science.

II. BRANCH PROGRAMS

A. Objectives

The primary mission of the Library Branch is to operate an efficient, comprehensive library in support of NIH scientific, medical, and administrative programs. Activities of the Library include selection, acquisition, organization, maintenance, and circulation of literature pertinent to the programs; operation of a photocopy service; provision of interlibrary loan service; provision of informational, reference, and bibliographical services; provision of Library services advisory assistance; and provision of a translating service for foreign scientific and medical literature. To fulfill its mission, the Library is responsive to changing literature needs of the NIH investigators, is knowledgeable of current developments in manual and machine methods of communication and information retrieval, and is alert to adjustment of procedures for improved Libra services.

B. Current Programs

Readers Services

The Circulation staff provides a charging system, making available books and journals which may be borrowed. The staff issues Library Identification Cards; operates the Library's security system; provides an overdue recall system; issues Pagemasters and makes assignments to locked carrels.

The Interlibrary Loan staff obtains from other libraries literature required by NIH investigators which is not included in the collection.

The Stacks and Copy Service staff maintains the stacks, carrels, reference, and Reading Room areas and reshelves books and journals to facilitate access by the Library clientele. A copy service is provided which allows greater use of the Library's journal collection.

Translating Service

The Translation Unit provides oral, recorded, and written translations as requested. Oral translations are emphasized in-house, and written translations are made for the most part by contractual firms.

Reference and Bibliographic Services

The Library Services Adviser program provides an integrated response to the information needs of the NIH scientific community. This may consist of utilization of external resources in addition to the resources and services available in the NIH Library, such as specialized information centers, computerized information retrieval systems, and clearinghouses. The

Reference staff supplies ready response to questions, verifies citations, and compiles short reference lists. The staff also mans the Reference Desks in the Reading Rooms. Senior Reference Librarians answer difficult reference questions and compile literature searches as requested. They serve as selectors for Library acquisitions by continually searching journals, publishers' catalogs, and announcements for literature pertinent to the scope of the Library.

Reference and Bibliographic Services Section staff provides bibliographic assistance with experienced searchers to formulate requests for MEDLARS and MEDLINE computer searches at the National Library of Medicine.

Technical Services

The Acquisitions staff provides for the acquisition of books, journals, technical reports, and microform materials by purchase, gift, and exchange which are pertinent to the scope of the Library. The staff is responsible for the maintenance of the Periodical Record, preparation of completed journals for commercial binding, and for the issuance of Current and Noncurrent Journals in the NIH Library.

The Cataloging staff organizes the acquired literature through classification, cataloging and subject heading, and processes it for inclusion in the collection. The staff is responsible for the maintenance of the catalog and the issuance of The NIH Booklist.

C. Program Progress and Accomplishments

Some physical alterations resulted in better arrangements for several staff areas on the Upper Level. The Branch Chief's office was moved, and other Office of the Chief changes provided space for this year's in-Library training program. A reception area and a consulting room were provided for the Library Services Adviser program in the Reference and Bibliographic Services Section. More space was added to the Section to regroup employees according to activities. The Readers Services Section was rearranged more effectively in less space. The Interlibrary Loan Unit was moved to give better availability to the NIH users of their service. New doors were fabricated to give necessary access from Technical Services Chief and Unit Head offices to their respective work areas.

A minor reorganization of the Library Branch was approved by the Director, DRS, effective June 28, 1971. The Stacks Maintenance Unit and the Duplication and Audiovisual Unit were consolidated into one Unit designated as the Stacks and Copy Service Unit under the Readers Services Section. The Reference Unit and the Bibliographic Unit were eliminated so that all activities of Reference and Bibliographic Services became the responsibility of the Chief of the Section.

Three Library Consultants to the NIH Library were appointed to advise the Branch Chief in the areas of Library automation and professional staff training. Mr. Glyn Evans, Coordinator of Library Systems, Five Associated University Libraries, Syracuse, New York, served as library automation consultant; Dr. Estelle Brodman, Librarian at Washington University School of Medicine, St. Louis, and Dr. Henry Dubester, professor at the Graduate School of Library and Information Science, University of Maryland, visited the Library concerning staff training needs for FY 1973. Reports on their findings and recommendations were made to the Branch Chief. Mrs. Evelyn Daniel, also from the Graduate Library School, University of Maryland, who conducted the Library's FY 1972 course for GS 5-6 Library Technicians, made recommendations for professional staff training based on questionnaires completed by the staff.

Nine staff members participated in the DRS Third Annual Equal Employment Opportunity Seminar this year entitled, Human Relations in Management, held October 20-22. In compliance with the Human Relations Seminar, decisions on a supervisory performance evaluation form for use by the employees supervised was prepared with the participation of the entire staff. Evaluations of supervisors were made at the same time as the annual performance review.

The initially-issued paper Library Identification Card was replaced by a blue plastic embossed card which alone has been honored since September 7 for obtaining Library services. Beginning July 1, 1972, a red plastic ID Card will be required. Registration is performed on an annual basis for regular NIH employees and on a continuing basis for new personnel.

Self-service copy provisions and a 24-hour copy service were introduced on July 1. Presentation of the Library Identification Card is required for the new services which are available on weekdays from 8:30 a.m. until 4:45 p.m. Requests may also be mailed to or deposited at the Circulation Desk as formerly for completion and mailing to the requester in about 5 days.

The Library Branch Training Program for FY 1972 was developed to meet individual and organizational needs according to the three group categories adapted for the FY 1971 training program. Meetings were held with each group to outline its training needs and the kind of training required to meet these needs. In the professional area the group elected the Section Chiefs to work with the Branch Training Chairman to carry out the FY 1972 program.

Group I, the professional group, chose training similar to last year's: attendance at NIH Lectures, pertinent in-Library seminars, and the opportunity for individual pursuance of academic courses. Several Section Chiefs were provided supervision and high level management courses designed for their development. Group II, GS 5-6, selected a planned course covering all aspects of library science. Such a course was designed and conducted by Mrs. Evelyn Daniel, a faculty member of the University of

Maryland School of Library and Information Science. Group III, GS 1-4, primarily desired enrollment in the library science courses for Library Technicians given in the evening at the U. S. Department of Agriculture Graduate School.

Two new trainee slots were established for the year. One slot was used for developing a Library Technician presently at the GS 5-6 level, to assume a relatively high nonprofessional position which did not exist in the NIH Library. The other slot was used for providing essential, individual on-the-job development of several GS 1-4 personnel to the level of duty performance required for the job at a higher level. This training was performed by a GS-12 professional staff member working closely with the respective supervisors.

Translating Service

Translating contracts covering the period April 1, 1972, through March 31, 1973, were awarded to five commercial translating firms. Two firms were awarded renewed contracts; the other three are new contractors.

Technical Services

Detailed studies were made to determine the feasibility of two computer systems for use in the Acquisitions Unit. Decision was reached to continue DCRT's WYLBUR system as applied to monograph ordering procedures. The PHILSOM system developed by Washington University School of Medicine Library was adapted for the journal control procedures.

A review was made of unbound journals in order to accelerate the recording of journal holdings for PHILSOM computer input. Missing issues have been listed for filling gaps, and many issues have already been obtained. Various categories of serials received by the Library have been identified, and decisions were made for more efficient methods of acquiring each category.

It is now possible to execute the two financial programs from the Library's WYLBUR terminal, alleviating former problems associated with improper handling of job control language and date in punch card format.

Readers Services

The Stacks Maintenance Unit and the Duplication and Audiovisual Unit were consolidated into one Unit designated as the Stacks and Copy Service Unit under the Readers Services Section as approved by the Director, DRS, effective June 28, 1971.

Two user registrations for Library Identification Cards were conducted during the year. On September 7, a blue embossed plastic card replaced the initially-issued temporary paper card for obtaining Library services.

Beginning September 7 also, the Library ceased the practice of mailing books and journals to requesters except for those with offices in off-reservation sites, such as the Wiscon and Westwood Buildings. Borrowers were asked to obtain and return Library journals in person. The present Library book deposit boxes located around the reservation remain in use and new and improved boxes will be obtained.

Reference and Bibliographic Services

As approved by the Director, DRS, effective June 28, 1971, the Reference Unit and the Bibliographic Unit were eliminated so that all activities of the Reference and Bibliographic Services Section became the responsibility of the Section Chief.

The Library Services Adviser program which was initiated in FY 1971 provides expert guidance in obtaining resources and services available in the NIH Library and other libraries which are pertinent to the individual research need. program broadens and integrates the reference and bibliographic services of the Library.

On-line bibliographic searching using National Library of Medicine's new MEDLINE computer system became possible at the NIH Library on March 22 with the installation of a MEDLINE terminal in the Upper Level Reading Room. Library staff trained in the MEDLINE system conducts searches for investigators, or gives instruction and guidance on use of the terminal. As in the past, bibliographic searches may also be made through NLM's MEDLARS system.

D. Problems

The major problem confronting the Library Branch revolves around personnel matters. Operation of the NIH Library with 1972 workloads and services but with a 1964 size staff would be a real challenge without the added difficulty of prevailing promotion freezes and grade de-escalation programs.

E. Program Plans

Increased attention will be given to the expansion of the Library Services Adviser program.

Completion and refinement of the Library automation systems in the areas of journal and monograph receipt and control will provide much benefit to both user and management.

The scope and coverage policy statement should be completed and available as the rational basis for the acquisition and retention of materials in the collection.

F. Publications

Stringer, A.G.: Career Counseling for Nonprofessionals. *Civil Service J.* 12: 7-9, 1972.
Journals in the NIH Library 1971. (Internal Use only) National Institutes of Health Library: *NIH Library Booklist*. Monthly (Internal Use only)

DIVISION OF RESEARCH SERVICES

Summary of Branch Activities July 1, 1971, through June 30, 1972

MEDICAL ARTS & PHOTOGRAPHY BRANCH Mr. Arthur F. Moore, Chief

I. SUMMARY

In spite of a reduction in personnel and an increase in demand for services, the Medical Arts & Photography Branch fulfilled most of its program commitments through the use of new and improved technology, wider training and a 75 percent increase in outside contract services. Through the application of advanced technology to our photography service, photomicrography output was doubled and an estimated 1,800 man-hours were saved in a variety of photo processes. More employees received more job-related training than in the previous year.

NIH LIBRARY

II. BRANCH PROGRAMS

A. Objectives

The objective of the Branch is to provide consultation and production services to the NIH; to visually communicate program effort and research results; to provide knowledge, skills, and techniques in visual design, medical art, applied arts, still photography, and cinematography for solving problems of recording, communicating, and presenting research activity; and to investigate, develop, and apply new visual techniques.

It is also the objective of the Branch in meeting NIH research program needs, to provide in-house services on a professional basis, competitive with commercially obtainable services at the lowest possible cost, and to develop specialized capabilities, particularly in graphic presentation, still photography, cinematography, and medical arts, tailored to NIH needs.

The Branch monitors procurement of art and photography services by outside contract, serving as technical adviser in obtaining needed additional services at the lowest cost consistent with high quality.

B. Current Programs

Programs of the Branch are still and motion picture photography, including photomacrography, photomicrography, high-speed cinematography, general photography, and related laboratory services; visual arts production, including publications design and general graphics; visual aids, including slides, vu-graphs, and other projectables; animation art work; technical, general, and medical illustration; exhibit design; statistical drafting, display charts; medical models; and computer-generated graphics.

C. Program Progress and Accomplishments

1. Major Accomplishments

The NIDR program entitled, "Studies of Oral and Pharyngeal Form and Function in Infants," was completed after four years and a cummulative total of approximately 2,200 hours spent on medical illustrations and dissections. This illustrative study describing development of form and function of pharynx and mouth of the human infant will be off the press July 1972.

A complete anatomy atlas of the male and female Rhesus monkey to be used as a workbook, autopsy protocol, was completed for Dr. Yound, a veterinary pathologist in the Department of Toxicology of NCI.

2. Operational Improvements

A new, faster and less expensive system for producing excellent film positives for color slides and overhead projections has been established with new equipment. Previously, film positives took several steps and about one hour to produce; now the same work can be done in two minutes at one-tenth the cost.

A 70mm copy camera system is now an integral part of the Branch photo production system. The quality of 70mm film has proven equal to that of the more costly 5 X 7 sheet film. It has increased efficiency to a point where the projected savings of 480 man-hours per year is being realized.

Increased availability of photomicroscopy is now possible with the acquisition of two new photomicroscopes. The previous two-week lead time for scheduling requesters has been reduced to five workdays. The new equipment will also expand the Section's technical capabilities.

The in-house modification of a microfilm processor capable of handling 100 ft. rolls of 35mm film for production of 2 X 2 slides has resulted in a 380 man-hour savings per year.

3. Service Contracts

With an increased demand for service at a time when there was a loss of personnel, the Branch used outside contract services more extensively. An increase of 75 percent in the use of such services over FY 1971 is a clear indication of a trend in the service operation of MAPB. Projections show increases in contracting will rise an additional 80 percent in the next three years.

The use of outside contracting by itself is not the total answer to increased quality production needs. Such contracting, to be creatively effective, must be scrupulously directed by a competent audiovisual person who will design and translate the raw information from the requester, precisely instruct the contractor on the work to be done, and conduct the necessary quality control once the work has been completed. Close clerical support is vital during all contract procedures to insure its fiscal integrity.

MAPB, during FY 1972, has developed an effective technique for the extended. use of contract services - a technique that will easily expand as conditions dictate.

4. EEO Developments

Equal employment opportunity goals continued to be pursued vigorously.

a. Five supervisors and four non-supervisory employees attended the DRS three-day fall Seminar on EEO.

b. Full report on this Seminar was made to a Branch-wide meeting.

c. All Branch staff meetings emphasize the importance first-line supervisors play in the EEO program.

d. A DRS counselor occasionally participates in Branch staff meetings.

5. Labor Relations

In May the Branch completed the first year of a two-year negotiated agreement with Local 2419 of the American Federation of Government Employees. Relations between management and Local 2419 were smooth and without incident.

6. Training

a. Twenty-eight members of the Branch received formal training in FY 1972. This figure represents an increase of four employees trained.

b. Two separate, unique training programs were instituted on MAPB premises during FY 1972. Mr. Joseph Paderewski, an eminent medical sculptor from the Shriners Hospital for Crippled Children, Galveston, Texas, and Mr. Robert Demarest of the Anatomy Department, Columbia University College of Physicians and Surgeons, New York City, conducted two-day seminars in February and May. Departing from the regular lecture route, these artists dealt directly with solutions to MAPB art problems. Eighteen artists of the Branch benefited greatly from these work sessions in plastic sculptor and air brushing.

The Branch, with professional abilities in certain areas at such a high level, will pursue further use of such seminars employing eminent audiovisual persons dealing with MAPB problems. The savings in dollars and specialized training received in problem areas where formal academic classes do not exist warrant continued development of this approach.

D. Problems

MAPB continues to urge its audiovisual counseling services on the NIH community. However, these services are far from fully used, and the Branch spends much unnecessary time in some hopeless patch jobs trying to save projects that were doomed from the start by incompetent conception. The Branch will vigorously pursue a course toward the position of one day having final authority to approve or disapprove audiovisual materials emanating from the NIH for distribution. Only upon reaching such a position will NIH be relieved of the unnecessary embarrassment it now suffers as a result of some of its audiovisual presentations.

E. Program Plans

1. Design layout and architectural drawings were prepared and approved in FY 1972 for the complete renovation of the Photo Lab area. Renovation construction will start and be completed in FY 1973.

2. MAPB has identified areas in which it plans research and development projects in line with the DRS-wide plan now in the development stage.

3. The Branch projects an increase of 50 percent in the use of outside contract services during FY 1973. This will allow MAPB to maintain a high level of quality and to meet the increase in demand for audiovisual services.

DIVISION OF RESEARCH SERVICES

Summary of Branch Activities July 1, 1971, through June 30, 1972

Veterinary Resources Branch Dr. Joe R. Held, Chief

I. SUMMARY

The name of the Branch was changed to more closely reflect its primary functions. These are to provide NIH investigators with living models and life support systems for biomedical research and to provide facilities and services related to the use of these models and systems.

Issues of laboratory reared and random source dogs were considerably higher than last year while colony reared and random source cat issues remained about the same. number of primates purchased and conditioned also remained at the same level. The primate breeding colony and the ungulate herd increased significantly. The use of experimental surgery services increased markedly and the use of facilities for the holding of experimental dogs increased slightly. Radiographic services decreased sharply. Rodent issues decreased slightly although contract purchases of noninbred rodents almost doubled. Tissue culture and media issues decreased slightly. Blood agar plate issues almost doubled--a feat made possible by automation. Issues of glassware remained approximately the same as last year.

The Animal Disease Investigation Service completed its first full year. During this period 128 calls were made to the various I/D's in addition to the routine clinical support provided within the Branch. Demand for this service continues to grow. At the request of I/D investigators a number of new inbred strains were added to the genetic repository. This activity has continued to grow in importance, not only in fulfilling NIH's needs, but also as a resource of breeding nuclei and reference animals for investigators throughout the world. As a first step towards providing better defined ungulates, a program of goat breeding was initiated. There was an increased use of ungulates for biologics production and research in various surgical procedures.

NIH LIBRARY

II. BRANCH PROGRAMS

A. Objectives

The primary objectives of the Veterinary Resources Branch are:

1. The issuance of research animals, animal biologics, tissue cultures, tissue culture media, bacteriologic media, and laboratory glassware.

2. The provision of facilities and professional staff for experimental surgery to include postoperative care and roentgenography and other special procedures.

3. The maintenance of animals during experimentation.

4. The acquisition of information, through research, on animal health, care, and husbandry.

5. The provision of consultative services on animal health and husbandry, use of experimental animals, tissue cultures, and bacteriologic media.

B. Current Programs

1. Production and Conditioning

a. Animal Production

A variety of rodents, rabbits, dogs, cats, and primates are bred and reared in the Branch's colonies. Some of these are characterized genetically and some are microbiologically defined. Care is taken to maintain the genetic integrity of inbred strains and minimize inbreeding of random bred stocks. Germfree and specific pathogen-free (SPF) rodents are produced for intramural research programs requiring them and for replacement breeders to enhance the health status of production and genetic colonies.

b. Animal Procurement and Conditioning

Primates, dogs, cats, and feral animals are procured and conditioned. Generally, these animals can neither be characterized genetically nor well-defined microbiologically; and they are of lower quality than NIH-bred animals, but their cost is less and they are adequate for many studies. These species are held for a period of several weeks before thay are issued, during which time they are clinically examined and tested for a variety of infectious agents. Treatments and immunizations are administered when indicated during the conditioning period.

Noninbred rodents are procured through contracts to supplement in-house production. They are delivered directly to NIH investigators. Quality control of these species is maintained through monitoring of the various producers' facilities and operations by Branch staff members.

c. Tissue Culture and Media Production

Several continuous cell line tissue cultures are maintained, propagated, and produced in large volumes to supplement I/D requirements not met by commercial sources or individual laboratory preparation. Media for the culture of bacteria, fungi, and tissue cells are produced to meet the needs of NIH investigators. A stringent quality control program insures that only high quality products, free of contamination and true to formulation, are issued. As a service to investigators, valuable cell lines are frozen and stored for long-term preservation.

d. Processing Laboratory Glassware, Animal Cages, and Miscellaneous Items

Laboratory glassware is decontaminated, sorted, cleaned, inspected, plugged, wrapped, sterilized, and issued to NIH investigators. The overall operation includes processing of used glassware received from investigators and the introduction of new glassware from replacement stock. In addition to cleaning animal caging for its own programs, the Branch furnishes cagewashing services to investigators in the Clinical Center, the Auburn Building, and the Patuxent River Laboratory. Clinical Center rubber-backed carpets are also washed. A service is provided for ethylene oxide sterilization of heat labile patient and laboratory equipment from the Clinical Center and other I/D's.

e. Animal Biologics Production

A dog blood donor colony is maintained for the production of A-negative blood for research use. Ungulates are maintained to produce a variety of antisera, blood, and tissue specimens for investigators. RIF-free and Marek's disease-free eggs used in NIH research are produced from flocks of chickens free of these agents maintained in isolators.

f. Genetic Repository

Genetically defined rodents that are valuable models in biomedical research are maintained to support I/D requirements and serve as a genetic repository for the international scientific community.

2. Experimental Surgery, X-ray and Related Activities

Facilities are provided for investigators to perform experimental surgery on any size domestic animal. These facilities include modern equipment for the proper anesthesia, handling, and physiological monitoring of experimental subjects under aseptic conditions. Upon request, staff veterinarians will perform special surgical procedures for investigators needing surgically prepared animals for their studies. Radiographic facilities and services are also made available for use on animals of any size.

3. Animal Holding

Dogs, ungulates, and germfree rodents are held for varying periods of observation while under test by NIH investigators. Provision is made for physiological sampling and collection of specimens.

4. Research and Disease Investigation and Control Within VRB.

The professional staff consists of persons trained in general clinical veterinary medicine and specialists in laboratory animal medicine, pathology, microbiology, epidemiology, genetics, nutrition, animal husbandry, mammology, and ecology. The efforts of these persons are oriented toward improving the Branch's programs by gaining new knowledge through research and the application of the best available procedures to meet the objectives of the Branch.

5. Consultative Services

Information and assistance is available to NIH investigators for the solution of problems relating to animal experimentation, health, care, and husbandry. Through the Animal Disease Investigation Service (ADIS) "house calls" are made to the I/D's to provide investigators with clinical veterinary services for their research animals. There is also a program in which the primary goal is to furnish each I/D a comprehensive review of its animal care programs with evaluations and recommendations for improvement. Consultative services are available regarding the use of tissue cultures and microbiologic medias.

C. Program Progress and Accomplishments

1. Change of Name

The name of the Branch was changed during the year to more closely reflect its primary functions. These are to provide NIH investigators with living models and life support systems for biomedical research, including research animals, tissue cultures, and microbiologic media. In addition, the Branch provides developmental and consultative services on the selection of research models, research animal housing and care, and techniques of animal experimentation. The Branch, both at its facilities in Bethesda and the NIH Animal Center in Poolesville, Maryland, provides NIH investigators wth facilities for the conduct of experimental surgery and the holding of research animals. The Branch also serves as a repository for animal strains with special heritable characteristics from which investigators throughout the world obtain breeding nuclei.

2. Production and Conditioning

a. Animal Production

Approximately 525,000 VRB-produced rodents and rabbits were issued to investigators, a reduction from 572,000 issued the previous year. The decreased level of production was not sufficient to meet investigator needs for animals, particularly inbred mice and guinea pigs. At mid-year, the overall percentage of nonreimbursable issues declined to less than 5 percent. This was an unrealistically low figure for animals for which there is a fluctuating demand and limited usage of one sex. Progress was made to establish hysterectomy-derived, barrier-maintained foundation colonies for all strains and stocks of mice. Of the 35 currently maintained inbred mouse strains, 33 were introduced into the barrier. Most strains adapted well to barrier conditions; however, reproductive failure was experienced in five strains. Over 100 hysterectomies were performed to establish a hysterectomy-derived, barrier-maintained, General Purpose mouse colony. To perpetuate the genetic diversity of this noninbred stock, 120 successful hysterectomies are necessary. A foundation colony of about 100 breeding pairs was established in the barrier. The barrier colonies will supply pathogen-free breeders to the production colonies.

Inbred and NIH mouse production colonies were converted from monogamous to harem matings to meet the requirements of the I/D's for these animals without increasing manpower.

A production room was established for raising noninbred complement-deficient (C-4) guinea pigs. This animal model was discovered as a mutant in the NIH guinea pig colony by a group of NIAID investigators in 1970. The colony has grown to a size of over 150 breeding females which produced about 1,000 animals for issue this year.

Noninbred guinea pig production was converted to a more efficient breeding system so that more offspring can be expected per breeding female and, at the same time, man-hours and space are conserved.

Because of reduced usage by investigators, production of Hartley guinea pigs was drastically reduced. CFW mouse production was discontinued because of limited usage and commercial availability.

An effort was made to improve the reproductive performance of the NIH rabbit while retaining its desirable large ears and veins and thin skins. Matings between NIH rabbits and disease-free animals from another colony were initiated, which should increase heterozygosity and productivity. The NIH colony had been closed since its introduction in 1933. An improved diet was formulated and tested in the rabbit colony. Methods and diets for the development of hysterectomy-derived rabbits were studied. An improved hand-nursing regime for hysterectomy-derived rabbits was developed, although digestive problems were not eliminated.

The canine breeding colony was culled to 96 bitches and 8 dogs. The primary criteria for culling was based on productivity, but undesirable conformation and disposition were also considered. Despite the culling, production was increased slightly from 885 pups in calendar year 1970 to 893 pups in 1971. Approximately 1100 colony-reared dogs were issued during FY 1972.

The cat breeding colony was maintained at 34 to 40 queens and 8 toms during FY 1972. Major improvements in the physical facilties included disposable cardboard queening boxes, cat-proofing of the kennels used for kittens, and improved cleaning techniques. Additional improvements and further reduction of the colony size is planned. Approximately 300 cats were issued during FY 1972.

To provide disease-free and better defined goats, a goat breeding program was initiated. Eight does and one buck presently make up the goat breeding herd. Approximately 15 kids were born during FY 1972. Goats produced from the breeding herd will be held until the age of one year before they are issued.

The primate breeding colony was enlarged to approximately 200 females.

b. Animal Procurement and Conditioning

Slightly less than 3,000 primates will be conditioned and issued this year, a level similar to that in FY 1971. The price of rhesus monkeys purchased under a new contract effective January 1, 1972, decreased by 33 percent from the previous contract. Mortality of newly imported monkeys during the conditioning period was 1.2 percent versus 6 percent for FY 1971.

Illness among animals was minimal and losses were virtually eliminated. The issue of dogs increased considerably during the first 6 months of FY 1972. Approximately 1300 random source dogs were issued. One hundred seventy foxhounds were purchased from outside sources to supplement the colony reared dog supply. Demand continues to exceed production capabilities. Purchase of foxhound type animals will continue at a low level.

The Primate Quarantine Building was occupied in January 1972 and all primate quarantine activities were transferred to the NIH Animal Center.

Slightly more than 2,000 random source cats are expected to be issued in FY 1972. This is the same as FY 1971. The cat conditioning program was changed during the year to include treatment of all cats for endo and ecto parasites.

Approximately 327 ungulate animals were purchased, quarantined and conditioned, and issued. In addition, 50 domestic fowl, including ducks, chickens, and turkeys were utilized.

Approximately 60,000 noninbred rodents were purchased from contractors this year compared to 37,000 in FY 1971. The increase resulted from a new contract for pathogen-free Swiss mice and increased usage of contract rats and hamsters. Contract mice have been received since January. Only a limited number of investigators have accepted the mice as replacements for the NIH raised noninbred stocks. Sprague Dawley rats and Golden Syrian hamsters continue to be supplied predominately by contractors.

c. Tissue Culture and Media Production

Based on the first six months of FY 1972, the number of requisitions processed for tissue culture and media will total 13,500; a slight decrease over last year. The volume of media produced will be 52,000 liters of bacteriologic media and 62,000 liters of tissue culture media for a total of 114,000 liters. This total represents a slight decrease over last fiscal year. In general, the decrease in the number of requisitions processed without a significant decrease in volume is indicative of a trend to larger volumes per requisition. Requisitions from the researchers for volumes of several hundred liters per requisition have not been uncommon.

Issues of blood agar plates of all types, including horse blood, sheep blood, and human blood plates will total 135,000 this fiscal year. This figure is almost twice the average number of blood plates purchased under a commercial contract, which was terminated during FY 1971. In addition to blood agar plates, a total of 365,000 plates of other types will be produced this year. Automation in media production made possible these significant increases.

The trend to issues of tissue culture cells in larger volumes, as cell suspensions, continued throughout the year. One hundred sixty-eight liters of cell suspension, sufficient in quantity for 168,000 tubes, were produced. As a result, issues of tissue cells in tubes decreased.

Additional liquid nitrogen storage equipment was added to keep pace with the demand for tissue culture cell freezing and storage services. The initiation of a charge for this service caused NIH investigators to become more selective in submitting cell samples for freezing and storage. This resulted in a reduction from 3,000 ampoules of cells frozen in FY 1971 to 2,000 in FY 1972.

A major change in the production of tissue culture media provides for bottling media directly from the sterilizing filter without the use of an intermediate collection reservoir. This change contributed to a continued low rate of contamination by eliminating an extra step in processing. In addition, a reduction in setup time was gained by eliminating the time-consuming tasks of rewashing and sterilizing large glass reservoirs.

A changeover to the use of ball mill ground powdered tissue culture media produced in-house was completed. In past years, several types of media used in large volume were purchased commercially as a powdered concentrate, but with the acquisition of large capacity grinding jars, the need to supplement production by commercial procurement was no longer necessary. After initial reluctance on the part of some investigators, the use of media prepared from powdered instead of liquid concentrates gradually became recognized as an accepted procedure. Many investigators now feel that a more uniformly staple media results from the use of the powdered media.

d. Processing Laboratory Glassware, Animal Cages and Miscellaneous Items

Glassware issues to the Institutes and Divisions will total about 10,610,000 pieces; almost the same number as last year. A total of 312,000 cages, racks, and associated pieces of equipment were processed, not including carpets washed for the Clinical Center.

An automated tube plugging machine capable of plugging four different size culture tubes at once was put into operation. Use of this machine enabled the Unit to increase the number of culture tubes by 91,000 over FY 1971.

A new disposable container for issuing pipettes was put into circulation and should eventually replace the stainless steel container now used. These disposable containers should eliminate the backlog of requests for pipettes in cans.

e. Animal Biologics Production

Domestic turkeys and ducks were utilized in small numbers to produce normal blood and antisera for specific research projects.

The canine blood donor colony was reduced through attrition to 240 animals. While this colony has a theoretical yield of 4080 units of blood annually, production losses during periods when issues are low are irretrievable. Since the demand for blood is quite variable, issues have not yet approached this level on an annual basis. The production of frozen plasma during slack periods to retrieve losses was relatively unsuccessful: investigators require fresh whole blood.

Biologics production from ungulate animals increased somewhat. Seventeen hundred liters of ungulate blood were produced. The size of the ungulate herd being maintained for all purposes increased by about 29 percent.

Eggs were acquired from inbred Line 6 chickens which were maintained in a barrier system and are RIF-free and susceptible to all Rous Sarcoma (RS) viruses (C/0). Males from this stock will be used to fertilize NIH hens, thereby producing embryos which are susceptible to all RS viruses.

3. Experimental Surgery, X-ray, and Related Activities

Activities in ungulate surgery increased considerably. Projects utilizing goats in a study of sleep and sheep in intrauterine fetal surgery generated 125 surgical procedures. Facilities are provided for postoperative observation and electroencephalographic recording of sleep patterns for goats with surgically implanted cranial electrodes.

The number of surgical procedures performed and the number of hours devoted to surgery increased. This year, 975 procedures were performed, which is a 40 percent increase over last year. Radiographic services decreased from 101 per month to 40 per month.

The long-term dog holding population has increased by 7 percent. Last year the average population was 290 dogs per month; this year the average monthly population is 310 dogs.

4. Genetic Repository

The genetic repository activity received increased emphasis. The rodent and rabbit colonies represent the most diversified multispecies rodent collection maintained at any centralized facility. In addition to supplying animals for intramural investigators, these colonies serve as a resource for the international scientific community. Many of the stocks, strains, and substrains are not available elsewhere and investigators throughout the world are supplied breeding nuclei. This year, approximately 70 investigators were provided with litters of inbred animals to start their colonies and several hundred noninbred animals were provided as breeders. This year, the Genetics Society of America gave recognition to this activity and recommended to NIH that it be expanded to serve as an all-inclusive genetic repository for rodents other than mice.

5. New Animal Models Program

A program was initiated in FY 1971 to assist investigators in obtaining new animal models to meet previously unfilled research needs. In some instances this involves the inclusion of new strains of existing laboratory animals exhibiting unique physiological or anatomic characteristics. In others it involves the adaptation from nature of animals having characteristics that might lend themselves to a particular research problem. New models are hysterectomy derived and foster nursed or hand nursed prior to introduction into the NIH colonies. Sixteen new strains or stocks were requested by NIH investigators for their research, and eleven of these were added to the repository.

Outdoor pens were erected at the NIH Animal Center for raising cottontail rabbits. Twelve cottontail rabbits were trapped and have been held to breeding age in these enclosures.

6. Animal Disease Investigation Service

Animal Disease Investigators made 128 calls involving consultations with numerous investigators from most I/D's. Animal species were varied and included rodents, rabbits, primates, carnivores, ungulates, and marsupials. The complexity of these calls also was varied and ranged from bite wounds in mice to controlling lymphadenitis in colonies of guinea pigs. This service seems to be well received and is growing.

7. Animal Nutrition

An open formula rat and mouse ration developed in FY 1971 was used in conventional mouse and rat colonies. Most investigators also converted their animals to the new diet. This diet is purchased through advertised bidding, thereby eliminating the necessity of sole source procurement. With the open formula, investigators know the percentages of each ingredient in the diet. Ingredient levels can be varied to meet the needs of a particular investigation or type of animal. In contrast, the formulation of commercial diets is secret. Conversion to the ration concludes almost two years of work on formulation of diets, controlled testing, testing under production conditions, specification writing, and informing investigators and feed manufacturers.

An improved open formula rabbit ration was formulated as a possible replacement for Feed A. The levels of fiber and vitamins were increased and protein was lowered in the new diet. Preliminary testing indicates a greater number of animals weaned when this diet is fed.

Studies comparing the performance of several commercially available puppy feeds continued throughout the year. Results from these studies will permit the development of an open formula diet to better meet the needs of pregnant and lactating bitches and pups.

8. Animal Health

An outbreak of fatal hemolytic anemia in 2-7 week old puppies in the dog breeding colony was diagnosed as babesiasis. The causative agent was identified in stained blood smears as Babesia canis. After an intensive tick eradication program clinical babesiasis quickly disappeared from the colony. Since no practical means was available for detection of subclinical cases, a serologic method for demonstrating specific antibody was developed utilizing the indirect fluorescent antibody technique. Splenectomized dogs were experimentally infected to produce heavily parasitized blood for use as antigen for the test. Sera collected at the time of the outbreak and afterwards will be surveyed.

Epizootic hemothorax of mice occurred in NIH colonies for the first time. As described previously in the literature, the disease appeared to be a noninfectious condition of male mice characterized by myocarditis and prolonged clotting and prothrombin times. Only barrier-sustained General Purpose mice were affected. The highest mortality, approaching 30 percent per month, occurred in mice at 10 to 14 weeks of age. Similar to the outbreaks in other laboratories, it disappeared before more extensive studies of the disease could be performed.

At approximately the same time that the hemothorax problem developed in mice, intrauterine hemorrhage became a serious disease problem in barrier-sustained Sprague Dawley rats, resulting in the death of nearly 30 percent of breeders reaching the age of 6 months. This condition, which is known to occur with much lower incidence in conventional rats, appears to be associated with premature placental separation. No abnormalities or clotting or prothrombin times were found.

Streptococcus zooepidemicus was isolated from diseased guinea pigs in animal rooms located in two NIH research laboratories, bringing the total number of known infected colonies at NIH to four. The infection has not been found in the NIH production colonies. Affected animals have chronic kerato-conjunctivitis, cervical lymphadenitis and, frequently, otitis media. The disease is considered a serious threat to research and very difficult to eradicate from heavily populated animal rooms. A variety of control methods are being tried including strict culling and sanitation procedures and administration of chloramphenicol. The causative agent, which was sensitive to sulfonamides when first isolated in NIH guinea pigs in 1969, is now resistant to sulfonamides. Epidemiologic studies are underway in an effort to discover the most likely source of infection and the most effective measures for control.

An outbreak of purulent cervical lymphadenitis and sinusitis occurred recently in the colony of random source cats. Thirty-two cases were recorded. A group G beta hemolytic streptococcus was consistently isolated. The agent was found to be sensitive to several antibiotics and was effectively treated with chloramphenicol.

Surveillance continues to demonstrate that exbreeder germfree, gnotobiote and barrier-sustained rats are now free of mycoplasma infection. This would indicate that previous recommendations for preventing such infections are effective.

Johnnes disease, which was found in seven goats in 1971, appears to be under control. Culture of feces from 123 goats and 80 sheep in 1972 yielded no isolations. Testing by culture of feces on mycobactin fortified media will continue indefinitely and will be used to screen all incoming animals prior to their introduction into the herd.

Diagnostic services for the rodent colonies were enhanced this year by the assignment of an experienced clinical veterinarian. A laboratory to provide diagnostic services for the colonies was established and approximately 700 necropsies were performed. The tissues of many specimens were examined for histopathology and received bacteriological follow-up.

D. Problems

Problems of animal disease are referred to elsewhere in this report. (See Part II, C, 8.)

There is a serious understaffing problem in spite of existing contracts to reduce levels of in-house production. The problem is further aggravated by the fact that many employees are attending authorized classes during working hours. To compensate for this shortage, many employees were required to work an unreasonable number of overtime hours, and several necessary activities, such as the increased production of Strain 2 guinea pigs, were postponed.

The prices for rodents were raised by 10 percent in the middle of the year to prevent a large revolving fund budget deficit. This indicates a need for financing research and development, new animal models, strain development, and repository activities from sources other than animal issues.

Attempts were made to improve physical working conditions for employees at the NIH Animal Center. The bulk of these efforts were directed toward improving Building T-8, which is the oldest major building at the Animal Center. Requests were initiated to improve the lighting and water pressure, to paint the interior of the building, and to make a variety of other repairs. None of these improvements have been made.

Lack of sufficient space to fully utilize all automated equipment for efficient media production continues to be a pressing problem. Cramped quarters for both personnel and equipment continue to contribute to morale problems. Efforts to expand services in areas such as tissue culture cell production had to be sharply curtailed because of inadequate space.

Transportation of completed media to outlying buildings on the NIH reservation continues to be unsatisfactory. On numerous occasions deliveries of media were lost or contaminated because of improper handling by inexperienced drivers who did not know the necessary precautions to take when handling biologic media. Until such time as the responsibility for the delivery of media is reassigned and the necessary personnel and equipment are made available, this problem will continue to occur.

Understaffing in the Glassware Unit, coupled with losses due to employees attending authorized training and educational classes, has created daily problems in meeting the demands for laboratory glassware. Increased use of overtime only partially compensated for these losses in manpower.

The return of improperly labeled, potentially hazardous, dirty glassware continues to be a problem, although some improvement was noted after presentation of a brief television film which was prepared by the NIH Safety Office. This film illustrates the problems associated with the handling of dirty glassware. It was shown to the Scientific Directors and a number of scientific and technical personnel from the various I/D's.

As in past years, a problem in the supply of sufficient metal trays for the return of dirty glassware continues. Daily complaints are received from investigators unable to get trays to sterilize and return their used glassware, even though an additional 600 new trays were placed into circulation.

E. Program Plans

Expanding quality control procedures to cover bacteriologic media as completely as the tissue culture media will be emphasized. Sampling of completed media and further in-line quality control checks will be increased.

Automation will be increased in glassware preparation by the addition of a flask plugging machine. Plans are underway to automate the handling of dirty glassware in the sorting area to improve potentially hazardous operations.

Studies are underway to determine which services must be curtailed to compensate for recent losses in personnel within the Glassware Unit.

A renewed effort will be made to locate some type of disposable container for the return of dirty glassware, although efforts in the past have been unrewarding.

The program to free all mouse strains and stocks of disease through hysterectomy derivation and barrier maintenance of foundation colonies will continue, as will the development of techniques for applying this practice to other species. This requires a cooperative effort in areas of nutrition, microbiology, and genetics and the development of methods for hand- and foster-nursing hamsters, rabbits, and guinea pigs. New strains of animals in danger of extinction and having significant potential for research will be added to the colonies. An attempt will be made to support these activities from the Management Fund rather than the Revolving Fund. This is necessary because the decreased in-house production activity can no longer support research, development, reference stock, and genetic repository activities and still maintain reasonable prices for animals produced.

A rodent research facility is planned that will provide centralized professional care for animals under investigation and technical assistance to investigators. This could alleviate overcrowded conditions in NIH animal research laboratories and best utilize space available in VRB. One building in the 14 complex could be devoted to this activity if positions are provided to utilize it.

The feasibility of providing increased quality control for animal feeds will be studied. Presently, the contractor is relied upon to establish nutrient content of ingredients and conduct estrogen assays. The possibility of contracting with an independent laboratory to assay feeds for estrogen and other toxic or infectious agents will be explored.

Open formula rations for autoclaving will be formulated and studied to decrease problems encountered in the barrier and provide defined diets for barrier-maintained animals.

The canine breeding colony will be expanded by purchasing quality dogs from outside sources. Hopefully, this will permit a rapid increase in the production capacity of the colony while introducing new blood lines to reduce the incidence of inbreeding.

The feline breeding colony will be reduced because there is little demand for colony-reared cats and staff levels have been reduced. Care will be taken during culling to minimize the loss of established genetic lines. Space vacated by the colony reduction will be used for the production of colony-reared dogs.

The dairy goat breeding herd will be slightly expanded if space and staffing limitations permit.

F. Publications

Ediger, R.D., Rabstein, M.M., and Olson, L.D.: Circling in mice caused by Pseudomonas aeruginosa. Lab. An. Sci. 21: 845-848, 1971.

Elman, L., Green, I., Judge, F., and Frank, M.: In vivo studies in C4 deficient guinea pigs. J. Exp. Med. 134: 162-175, 1971.

Ganaway, J.R., Allen, A.M., and Moore, T.D.: Tyzzer's Disease. Amer. J. Path. 64: 717-730, 1971.

Hansen, C.T., and McEleney, W.J.: Strain and Season differences in the reproductive performance of inbred mice, rats, and guinea pigs. Proc. IV ICLA SYMPOSIUM, NAS: 179-202, 1971.

Held, J.R. and Lopez-Adaros, H.: Complaciones neurologicas posteriores a la administracion de vacuna antirrabica de cerebro de raton lactante. Bol. Ofic. Sanit. Panamer. 71: 50-59, 1971.

Potkay, S.: Postoperative management of experimental thoracic surgery in the dog. Lab. An. Sci. 21: 234-241, 1971.

Potkay, S. and Palmer, A.C.: Effects of chloramphenical on barbiturate and halothane anesthesia in rhesus monkeys, (Macaca mulatta). Lab. Prim. Newsletter, 10: 11-14, 1971.

III. INDIVIDUAL PROJECT REPORTS

Serial No. DRS-VRB-1
1. Veterinary Resources Branch
2. Comparative Pathology Section
3. Bethesda

PHS-NIH
Individual Project Report
July 1, 1971, through June 30, 1972

Project Title: CHRONIC RESPIRATORY DISEASE OF THE LABORATORY RAT

Previous Serial Number: DRS-LAB-1

Principal Investigator: James R. Ganaway

Other Investigators: Anton M. Allen
Thomas D. Moore

Cooperating Units: Rodent and Rabbit Production Section

Man Years:

Total: 0.3
Professional: 0.3

Project Description:

Objective: To determine the character, cause, and means of preventing this disease complex.

Major Findings: Mycoplasma infection was detected in germfree rats a little over two years ago. Studies indicated that the infection was probably endemic in the germfree rats for several years prior to this finding. Additional study in this laboratory demonstrated the superiority of the oropharynzed swab technique as a sensitive means of detecting *Mycoplasma pulmonis* infection in the living rat. With the working hypothesis that the infection was introduced into the germfree isolators via the infected uterus of hysterectomized near-term dams, recommendations designed to prevent further occurrence of this infection in germfree rats were submitted to the Rodent and Rabbit Production Section. Surveillance of discard exbreeder rats from germfree and gnotobiote maintained isolators, and from similar rats received from the barrier-maintained production colony during the past year indicate that the previously submitted recommendations were effective in that all rats examined have been free of this infection.

Significance: CRD continues to be the greatest cause of morbidity and mortality in laboratory rats. The etiology remains obscure. Our studies provide an elucidative basis for the "rumors" that respiratory disease of unknown cause occurs in germfree rats. Our studies may also help to clarify the role of Mycoplasma pulmonis infection (recently purported by other investigators as the cause of CRD) in the complex etiology of CRD of laboratory rats.

Proposed Course: Continuation

Honors and Awards: None

Publications: Manuscript is in preparation.

Serial No. DRS-VRB-2
1. Veterinary Resources Branch
2. Comparative Pathology Section
3. Bethesda

PHS-NIH
Individual Project Report
July 1, 1971, through June 30, 1972

Project Title: TYZZER'S DISEASE

Previous Serial Number: DRS-LAB-2

Principal Investigator: James R. Ganaway

Other Investigators: Anton M. Allen
Thomas D. Moore

Cooperating Units: None.

Man Years:

Total:	0.5
Professional:	0.5

Project Description:

Objective: To characterize the etiologic agent. To study the pathogenesis of the disease through experimental transmission studies. To recommend measures for the control and/or prevention of the disease.

Methods Employed: Microbiology and Pathology

Major Findings: The disease continues to occur endemically in the NIH rabbit production colony. Continuing studies are designed to characterize the etiologic agent, *Bacillus piliformis*. Though a method has been found to produce spore-free suspensions, studies have been hampered by the extremely unstable nature of the vegetative bacillus and the inactivating effect of standard storage techniques (such as lyophilization or freeze and storage at -70 degrees C). A wide range of stabilizing effects have been found among a variety of diluents tested.

Significance: This disease is emerging as a common, often fatal, enteric infection of a variety of laboratory animals including mice, rats, hamsters, gerbils, rabbits, cats, and monkeys. The etiologic agent is a most unusual one whose collective characteristics have no equal in the field of microbiology and, consequently, is unclassified at present. Much of our present day information on the widespread occurrence of the disease in a variety of animal species was stimulated by our report of the disease in rabbits, this being the first record of the spontaneous occurrence of the disease in a species other than the mouse.

Proposed Course: Continuation

Honors and Awards: None

Publications: None

Serial No. DRS-VRB-3
1. Veterinary Resources Branch
2. Comparative Pathology Section
3. Bethesda

PHS-NIH
Individual Project Report
July 1, 1971, through June 30, 1972

Project Title: PASTEURELLA IN GNOTOBIOTIC RATS

Previous Serial Number: DRS-LAB-3

Principal Investigators: Thomas D. Moore

Other Investigators: Anton M. Allen
James R. Canaway

Cooperating Units: Pathogen-free Animal Production

Man Years:

Total: 1.0
Professional: 0.3
Others: 0.7

Project Description:

Objective: To ascertain the role and incidence of P. pneumotropica in gnotobiotic, barrier-maintained rats free of respiratory illness. To determine the preferred location of this organism in experimentally inoculated germfree rats.

Methods Employed: Microbiology and pathology

Major Findings: P. pneumotropica was isolated from the inflamed small intestine of inbred, gnotobiotic rats maintained in a closed barrier system. Further investigation and more extensive culturing showed the presence of this agent in all barrier room rats and mice as well as in a number of germfree isolators. An examination of healthy, female Sprague-Dawley rats from the barrier revealed that the organism had colonized the intestine with the caecum as the preferred site. The respiratory tract in these naturally infected rats was free of the organism while the uterus was culturally positive sporadically. These findings were generally confirmed in experimentally infected, germfree rats inoculated per os. In this latter case, occasional isolations were made from the trachea but definite colonization of the gut occurred with an increase of organisms with time. Again, isolations from the uterus were sporadic. Further experimental infections with this agent in germfree rats inoculated by nasal instillation and by aerosolizature failed to produce any signs of respiratory disease, either clinically or microscopically. Again, the organism was isolated consistently from the caecum and sporadically from the lung and trachea. Control germfree rats placed in contact with the above rats were shown to carry the organism in their caeca.

Significance: *P. pneumotropica* has been implicated as an etiologic agent in respiratory disease in mice and rats. The organism has been described as having an affinity for tissues of the respiratory tract although it has been isolated from brain, uteri, and spleen of mice. More recently, it has been isolated from eye abscesses in conventional mice here and in two other colonies. More information on the relationship and role of this organism in rodent disease is important.

Proposed Course: Continuation

Honors and Awards: None

Publications: A manuscript is being prepared.

Serial No. DRS-VRB-4
1. Veterinary Resources Branch
2. Comparative Pathology Section
3. Bethesda

PHS-NIH
Individual Project Report
July 1, 1971, through June 30, 1972

Project Title: FLUORESCENT ANTIBODY TECHNIQUE AS A SEROLOGIC MEANS OF DETECTING *BABESIA CANIS* INFECTION

Previous Serial Number: None

Principal Investigator: James R. Ganaway

Other Investigators: Anton M. Allen
Thomas D. Moore
Stephen Potkay

Cooperating Units: Carnivore Unit, Animal Center Section

Man Years:

Total:	0.4
Professional:	0.4
Others:	0.0

Project Description:

Objective: To determine a means of detecting *Babesia canis* infection in the intact or non-splenectomized dog.

Methods Employed: Parasitology and Immunology

Major Findings: The indirect fluorescent antibody technique was utilized as a quantitative serologic means of detecting antibody to *Babesia canis*. Films of air-dried, non-fixed, infected red blood cells on microscope slides were found to retain antigenicity after extended periods of storage at -70 degrees C.

Significance: During the past year, *Babesia canis* infection was diagnosed as the cause of death in puppies born at the Animal Center. The only known reliable means of detecting this infection in mature dogs is the microscopic examination of giemsa-stained blood films taken from dogs following splenectomization and immunosuppression. Though the examination of stained blood films taken from clinically normal intact dogs is unlikely to yield evidence of parasitemia, this method was used to provide evidence that the infection was endemic in the breeding and blood donor colony dogs at the Animal Center. Though immediate steps were taken to control the parasitic vectors (ticks), the problem of chronic infection remains and the effect of this infection upon the canine blood donor program remains unknown.

Proposed Course: Completed

Honors and Awards: None

Publications: None

Serial No. DRS-VRB-5
1. Veterinary Resources Branch
2. Rodent and Rabbit Production Section
3. Bethesda

PHS-NIH
Individual Project Report
July 1, 1971, through June 30, 1972

Project Title: GENETIC ANALYSES AND DEVELOPMENT OF NEW STRAINS FOR BIOMEDICAL RESEARCH

Previous Serial Number: DRS-LAB-5

Principal Investigator: C. T. Hansen

Other Investigators: K. P. Smith
W. J. McEleney
W. J. Hinkle

Cooperating Units: Laboratory of Bacterial Products, DBS
Laboratory of Immunology, NIAID
Laboratory of Pathology, GLC, NCI
Laboratory of Biology, GLCI NCI
Laboratory of Microbial Immunity, NIAID

Man Years:

Total:	1.0
Professional:	0.5
Others:	0.5

Project Description:

Objective: 1) To study the role of genetic and environmental components involved in the dynamics of reproductive performance of inbred strains of animals, 2) to conduct genetic monitoring of inbred strains, and 3) to develop new animal models utilizing the existing gene pool and new and exotic species.

Methods Employed and Major Findings: Analysis of long-term reproductive records of inbred strains has shown that the most important component of reproductive yield is the frequency of litters weaned rather than the more traditional average litter size at weaning. The frequency of litters weaned is determined by both genetic and environmental factors.

Studies are underway to establish characteristic strain frequencies of various tumors and age of onset of leukemias in both SPF and conventional environments.

Blood pressure levels of inbred rat strains are being monitored. The range in systolic blood pressures of 17 inbred strains is from 116 mm hg to 182 mm hg in males at 10 weeks of age. F1 hybrids of these strains demonstrate that blood pressure is inherited in a complex manner.

Selective breeding for the sensitivity and resistance to effect of histamine after treatment with B. pertussis has reached the thirteenth generation. Sensitivity has been increased to about 75 percent in the sensitive strain and decreased to about 3 percent in the resistant strain from an average sensitivity of 30 percent in the unselected base population.

A number of oriental mouse species have been introduced into the colonies for the purpose of studying additional genotypes involved in the immunoresponse mechanism.

The development of closed lines of rabbits continues. Four lines have been established homozygous for a pair of genes which control the gamma globulin allotypes. Work has been undertaken to study the inheritance of tissue antigens in these species. Also, preliminary analysis of long-term reproductive records has also been undertaken in rabbits.

Significance: The significance of these projects is to develop, by the use of genetic techniques, animal models which have an application to biomedical research.

Proposed Course: Continuation

Honors and Awards: Dr. Hansen was invited to present a paper entitled, "A Genetic Analysis of Hypertension in the Rat," at the U.S. Japan Symposium on the spontaneously Hypertensive Rat in Kyoto, Japan, October 1971.

Publications: Hansen, C.T. and McELeny, W.J.: Strain and season differences in the reproductive performance of inbred strains of mice, rats, and guinea pigs. Proc. IV ICLA Symposium, NAS, 179-202, 1971.

Serial No. DRS-VRB-6
1. Veterinary Resources Branch
2. Rodent and Rabbit Production Section
3. Bethesda

PHS-NIH
Individual Project Report
July 1, 1971, through June 30, 1972

Project Title: DEVELOPMENT OF DIETS FOR LABORATORY ANIMALS

Previous Serial Number: None

Principal Investigator: J. J. Knapka

Other Investigator: F. J. Judge

Cooperating Units: None

Man Years:

Total:	2.0
Professional:	0.5
Others:	1.5

Project Description:

Objectives: 1) To formulate and evaluate open formula rations designed to improve the nutritional status of laboratory animal colonies, 2) to accumulate data regarding the specific nutrient requirements of various strains of inbred laboratory rodents.

Methods Employed: A series of factorial designed feeding trials are conducted to determine the effect of various diets differing in nutrient concentrations and physical form on the growth and reproductive performance of the species involved. Criterion of evaluation includes number of pregnancies, number of litters born, number of litters weaned, number of offspring weaned, weight of offspring weaned, and the post-weaning growth rate of offspring. These data are coded for computer analysis by the appropriate statistical methods.

Major Findings: An open formula diet for conventional rats and mice was formulated and tested. The performance of rodents fed the new diet was equal to those fed a commercial diet. An open formula diet for rabbits has been formulated and is being evaluated. Preliminary analysis of data from this testing indicates that increased litter size at weaning can be expected from the new diet.

Significance: The development of open formula rations for NIH production and research animal colonies is advantageous because 1) production of rations is not restricted to a single mill in the event of a fire or bacterial contamination, 2) investigators have the opportunity to know the complete nutritional status of animal colonies, 3) a basis is provided for the improvement of rations for particular stocks or strains of animals, and 4) competititve procurement of essentially the same product can be accomplished over many years.

Proposed Course: Continuation

Honors and Awards: None

Publications: None

Serial No. DRS-VRB-7
1. Veterinary Resources Branch
2. Animal Center Section
3. Poolesville

PHS-NIH
Individual Project Report
July 1, 1971, through June 30, 1972

Project Title: A COMPARISON OF PHYSICAL AND HEMATOLOGIC CHARACTERISTICS OF PUPPIES FED DIETS CONTAINING 9%, 8%, and 6% FAT

Previous Serial Number: DRS-LAB-7

Principal Investigator: Stephen Potkay

Other Investigators: Joseph J. Knapka
Amos E. Palmer
Terry Pitts

Cooperating Units: Rodent and Rabbit Production Section

Man Years:

Total:	0.8
Professional:	0.2
Other:	0.6

Project Description:

Objective: To determine the relative values of feeds containing three levels of fat as diets for puppies during the weaning and growing periods.

Methods Employed: 1) Matings were scheduled so as to produce litters of genetic uniformity. 2) Thirty litters of pups (Foxhounds) were equally divided into three groups which were fed commercial dry diets containing 6 percent, 8 percent, and 9 percent fat, respectively. Dams were fed the same diets as their puppies beginning two weeks prior to parturition and continuing through weaning. 3) Supplemental feeding, which consisted of reconstituted canned milk, was provided uniformly for puppies to expedite weaning. The dry feeds were provided ad libitum for all bitches and their litters. 4) Evaluations consisted of examining and weighing each bitch weekly through weaning and each puppy weekly until 20 weeks of age. Measurement of hematologic values was done by standard methods, samples were obtained weekly from three randomly selected puppies from each litter and from their dam.

Major Findings: Final evaluation is awaiting computer analysis.

Significance: The majority of commercially available diets are in compliance with the minimum nutritional requirements for dogs as stated by the National Research Council, Committee on Animal Nutrition. However, these diets differ markedly in providing usable or digestable nutritives to puppies. The differences are evident from observations of general physical condition, weight gain, and hematologic values of dogs given these feeds. Future selection of diets for growing puppies will be based in part on the information concerning dietary fat content which is derived from his study.

Proposed Course: Work completed. Data is being analyzed.

Honors and Awards: None

Publications: None

DATE DUE

GAYLORD

PRINTED IN U.S.A.

LIBRARY
NIH
Amazing Research.
Amazing Help.

http://nihlibrary.nih.gov

10 Center Drive
Bethesda, MD 20892-1150
301-496-1080

NIH LIBRARY
4 0108 3566

BOUND BY

NIH LIBRARY
3 1496 00178 5008